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Your Questions answered

Readers may send questions from their own practice or other medical problems which will be answered by qualified consultants. Replies are forwarded by mail immediately and selected questions and answers are published each month in this section.

• SINUSITIS

Q. Is NEO-GUISODIDE® used to treat acute or chronic sinusitis?

M.D.—Montana

A. Solutions having astringent and hygroscopic properties may be applied topically in the nose on cotton pledgets for 10 to 20 minutes. These applications promote emptying of the mucous glands and shrink swollen mucosa, which usually is not subject to secondary swelling.

• ULTRASONIC THERAPY IN ARTERIOSCLEROSIS OBLITERANS

Q. A 67 year old woman who has had arteriosclerosis obliterans of the left foot for the past eight years had a lumbar sympathectomy one year ago and has not walked since that time. There is a minimal amount of swelling and occasional bluish discoloration in the foot; however, there is no appreciable difference in the temperature of the foot and that of the leg or the other foot. There are no posterior tibial or dorsalis pedis pulsations; the femoral pulse is adequate. The patient has almost continuous pain. Therapeutic measures have included elevation, warm soaks and administration of quinine, various analgesics and PRISCOLINE®.

Would ultrasonic therapy be helpful in relieving the pain? Is there any contraindication to using it in this case?

M.D.—Massachusetts

A. There is no rationale for using ultrasonic therapy in a patient with the symptoms described.

• CARDIAC MURMUR

Q. A 12 year old boy has a soft blowing, grade II to III apex murmur which has been heard on several occasions. An electrocardiogram has not been taken; however, a roentgenogram showed no enlargement of the heart, and there is no history of rheumatic fever. The patient does not have cyanosis or clubbing of the fingers, and his size is normal for his age. His blood pressure is 120/70.

Should this patient be allowed full participation in sports? He has played hockey previously, with my consent, and has had no difficulty. Should further studies be made?

M.D.—Minnesota

A. This patient may be allowed full participation in sports. However, he should have a cardiac x-ray examination with the barium swallow, and a physical examination at least once a year.

• FORGETFULNESS

Q. Is there any treatment for the forgetfulness of old age?

M.D.—Alberta

A. No curative treatment is known for forgetfulness in old age. It is sometimes possible to compensate for it by using specific notes and other devices to aid the memory. If the forgetfulness is severe, it may be helpful to restrict the patient's activities so less strain is placed on his memory. The patient must make a major attempt to adapt to and live within his abilities.

(Continued on page A-22)

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• **SYNOVECTOMY**

Q. For 35 years, a 73 year old physician has had rheumatoid arthritis of the left knee joint, confirmed both clinically and roentgenologically. The initial attacks were mild and of two or three weeks' duration, with remissions lasting from three to six years. About seven years ago the attacks became more severe and the first tapping was done, without affording much relief. Although orally administered cortisone was to some degree effective, it was discontinued on the advice of a cardiologist because of disturbing retrosternal discomfort. In January 1953, the patient was given intra-articular injections of cortisone, later changed to hydrocortisone and ARISTOCORT®. Excellent results were obtained; remissions lasted from six to eight weeks, with one as long as a whole year. However, the condition has become progressively worse in the last 9 to 10 months. Due to more rapid accumulation of fluid, tapping and injections have been necessary every 10 to 14 days. Swelling and soreness of the joint have caused an uncontrollable limp. An x-ray taken in February 1958 showed progressive narrowing of the joint space, with some sclerotic changes in the blood vessels of the joint area.

During these years, the patient has always been active and has had a good appetite. He weighs from 135 to 140 lb. and is 62 in. in height. He consulted an orthopedic surgeon who recommended a synovectomy as the only solution, assuring him of a favorable outcome. Would you advise me regarding the (1) nature and procedure of the operation; (2) indications and contraindications; (3) statistical data concerning the results; and (4) average time required from the day of the operation to recovery of the function of the knee joint.

M.D.—Pennsylvania

A. "Synovectomy" means operative removal of the synovial membrane. It is usually performed through an anteromedial parapatellar incision. Occasionally, a posterior incision is needed in addition to the anterior approach. Proceeding from above downward, the surgeon removes the entire synovial membrane. Removal of the semilunar cartilages is optional, depending on their condition. All pannus and other pathologic tissues are carefully removed. Postoperatively, a soft compression dressing and splint are applied for 10 days.

The indications for operation are a thickened capsule and synovium, with an increase in articular fluid, which fail to respond to conservative treatment. Apart from those contraindications applicable to the general physical vigor of the patient, excessive destruction of the bony and cartilaginous surfaces precludes operation.

Results of the operation depend to some extent on the degree of activity of the disease. Satisfactory results are obtained in 85 per cent of patients with a normal sedimentation rate, but in only 60 per cent of those with an elevated sedimentation rate. Although pain and discomfort are, as a rule, greatly relieved by the operation, increase in the range of motion is rarely achieved.

The average time involved from the day of operation to recovery of knee function varies considerably, depending on the patient's persistence in carrying out the active exercises required to return the quadriceps muscle to nearly normal strength. A period of about three to four months is usually required.

• **COXA PLANA**

Q. I would like information on the treatment of coxa plana and a list of recent literature on the condition.

M.D.—Alabama

A. Coxa plana, also known as Legg-Calvé-Perthes disease, is the most common of the osteochondroses affecting children and young people. Treatment is directed toward preventing collapse and deformity of the femoral head after the condition has healed. The patient must follow a nonweight-bearing regimen for a period varying from one and a half to five years, depending on the severity of the disease, the patient's age at onset, and the quadrant of the femoral head most severely involved in the disease process. The average period required is three years. Nonweight-bearing may be attained by elevating the opposite shoe or using crutches, braces or a sling to keep the knee on the involved side flexed so that weight cannot be borne on the foot. From a theoretical standpoint, at least, modified recumbency probably is the best treatment for the involvement of one hip and is the procedure of choice when both hips are involved.

The most recent complete publication on this condition is "Legg-Calvé-Perthes Syndrome and Related Osteochondroses of Youth," by Charles Weer Goff, M.D., published in 1954.

What's happening in Medicine ?

POSTGRADUATE MEDICINE'S REPORT of late news of interest to practicing physicians

NEW DIAGNOSTIC TECHNIC FOR VARICES

Radiological Society of North America:

- A new diagnostic method, using compression of esophageal varices by an intraluminal balloon and injection of barium below the balloon, has given improved radiologic results in a preliminary study on 24 patients. Routine roentgenologic methods fail to reveal about 50 to 80 per cent of varices. The new method promises to reduce the associated high mortality rate.—Dr. M. A. Nathan, Jefferson Davis Hospital, Houston.
- Roentgenologic examination offers the best chance for obtaining a precise diagnosis of staphylococcal pneumonia early enough to offer some hope of altering the high mortality rate, which at present is more than 50 per cent.—Dr. Harvey I. Meyers, Los Angeles.
- Clinical data covering a 33 year period on several hundred married women treated by irradiation for infertility has revealed minimal genetic effects among their 587 children and 44 grandchildren. Only three children had abnormalities; the grandchildren had none. Adverse criticism of radiation based solely on animal experimentation cannot properly be extrapolated for results in human beings.—Dr. Ira I. Kaplan, New York.
- Although cinefluorography offers great promise in understanding disease processes, some specific advances in technical devices are needed before this procedure assumes a major role in diagnostic medicine. The future depends largely on developments in the field of image intensification.—Dr. Lee B. Lusted, Rochester, N.Y.

LOW-FLOW PUMPING TECHNIC

American Association for the Advancement of Science:

- Procurement of blood for transfusion and priming of pump-oxygenators for congenital cardiac surgery is difficult. The need for reduced flow rates of blood, reduction in the body's metabolic requirements by lowering body temperature, and pharmacologic agents to lower tissue demands for oxygen has become apparent.—Dr. Denton A. Cooley, Baylor University College of Medicine, Houston.
- The embryo becomes sensitive to x-rays in the first few days following conception, usually before the woman is aware of pregnancy. Studies indicate that fetal damage can start long before the onset of the midtrimester. Pelvic x-rays of women in the reproductive age should be avoided.—Dr. Roberts Rugh, Columbia University College of Physicians and Surgeons, New York.

Ban on tonsillectomies

American Laryngological, Rhinological and Otological Society:

• In view of the variability of immune response to Salk vaccine, it is unwise to ease the present ban on tonsillectomies and adenoidectomies during the summer season. Surgical stress also may alter the infective capacity of the virus and the immunologic capacity of the host.—Dr. Saul Krugman, New York University College of Medicine, New York.

New oral agent for dermatomycoses

American Academy of Dermatology and Syphilology:

• Early clinical trials of the oral antibiotic griseofulvin indicate a major advance in the conquest of dermatomycoses. Infections of 10, 20 or even 50 years' duration seem to respond as readily as those present for a few weeks or months. Safety of internal administration has been demonstrated in mice, guinea pigs, rats, cats and monkeys. Keratin-producing cells seem able to resist fungal attack. A daily dose of 1 to 2 gr. appears to be adequate, although the minimal effective dose and the optimal dose have not been established. Likelihood of relapse or recurrence of infection is still unknown.—Dr. Harvey Blank, University of Miami School of Medicine, Coral Gables.

"Anorganic" bone graft successful

American Academy of Orthopaedic Surgeons:

• Anorganic bone used in surgical procedures on 40 patients, who were followed from five months to two years, shows good toleration and rapid incorporation in reparative callus at an early stage. Results were unfavorable in only one patient. Anorganic bone consists largely of the crystalline-mineral latticework of bone. It can be shaped with a scalpel to fit contours of any bone defect.—Dr. Lloyd A. Hurley, New York.

• Tumor-bearing areas have been isolated and perfused in 37 patients with malignant tumors involving the upper and lower extremities. Agents used have been nitrogen mustard, phenylalanine mustard, thio-TEPA and actinomycin D. The dosage is six to eight times the usual systemic dose. Of 13 patients with malignant melanomas, the disease is considered quiescent in three, controlled in four, and recurrent in four. Two patients have died.—Dr. Edward T. Krementz, New Orleans.

• Any patient less than 55 years old with compression fracture and demineralization should be thoroughly examined since only about one in six of such patients has osteoporosis. Analysis of 105 patients showed malignancy was present in about 50 per cent of cases.—Dr. James A. Nicholas, Hospital for Special Surgery, New York.

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Conference on Plasma Proteins and Cellular Elements of the Blood:

• Plasmapheresis, a process by which blood is taken into the Cohn-ADL Fractionator where cells are separated from plasma and then reinfused into the donor, has been carried out weekly for nine months among 10 donors without ill effects. The donors have shown no significant changes in red blood cell count, hemoglobin level or platelet count.—Dr. Hugh M. Pyle, Protein Foundation, Cambridge.

• Red blood cells separated from plasma, mixed with glycerin, and stored in the frozen state showed a viable yield as high as 77.3 per cent for 18 month old blood and 93.8 per cent for six month old blood.—Dr. Achot Khoubesserian, Protein Foundation, Cambridge.

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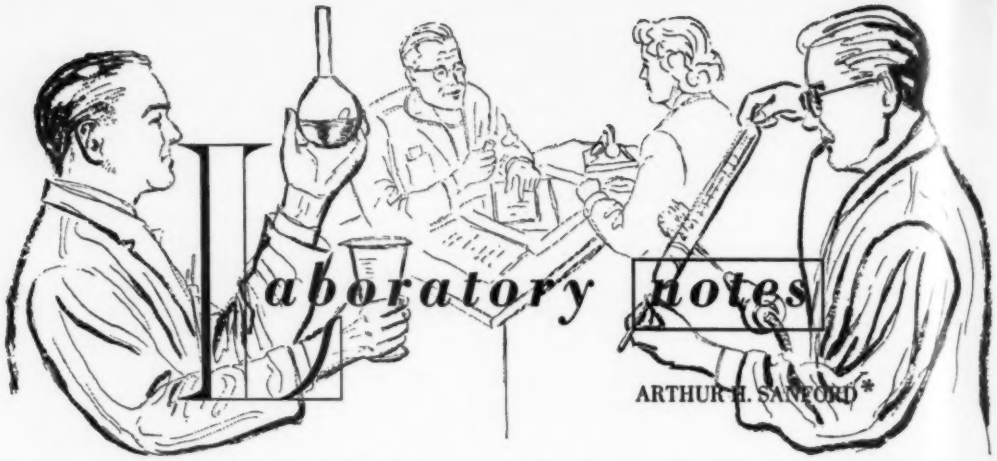

I am pleased to devote this month's column to the following discussion of investigative procedures for diagnosing bleeding disorders. This discussion will be published in two parts, the second part to appear next month.—Arthur H. Sanford, M.D.

Laboratory Aids in Diagnosis of Bleeding Disorders

SHERWOOD P. MILLER†

City of Hope Medical Center, Duarte, California

SHERWOOD P. MILLER

WHEN bleeding results from a hemorrhagic diathesis, it can be an extremely fascinating diagnostic problem. If, in addition to a healthy curiosity, one has a moderate amount of time, a few test tubes and stop watches, and access to a water bath, it is not too difficult to arrive at an etiologic diagnosis. Most clinical bleeding disorders may be diagnosed by relatively simple laboratory procedures. Even the rarer entities may be diagnosed with a minimum of equipment, although patience and precision may be required. Bleeding disorders are due either to a capillary-platelet defect or to a deficiency of some plasma factor known to be required for normal coagulation. The relationship between these two groups of disorders is illustrated in figure 1.

The normal reaction of small vessels to trauma is spasm, which provides for a temporary arrest of blood flow and allows time for a local accumulation of the factors responsible for coagulation. Vasospasm is followed in a few minutes by vasodilatation. Normally, a firm clot will have been formed at the site of injury during this period, so that hemostasis is effectively established. If a capillary defect exists, the normal arrest of blood flow does not occur and bleeding persists. Local accumulation of coagulation factors is not possible. Since the platelets are among the most important factors in plugging the vessels, a deficiency of platelets, quantitative or functional, will have

(Continued on page A-40)

*Emeritus Staff, Section of Clinical Pathology, Mayo Clinic; Director of Laboratories, Rochester State Hospital, Rochester, Minnesota.

†Formerly Chief, Coagulation Service, City of Hope Medical Center, Duarte, California, now in Staten Island, New York.

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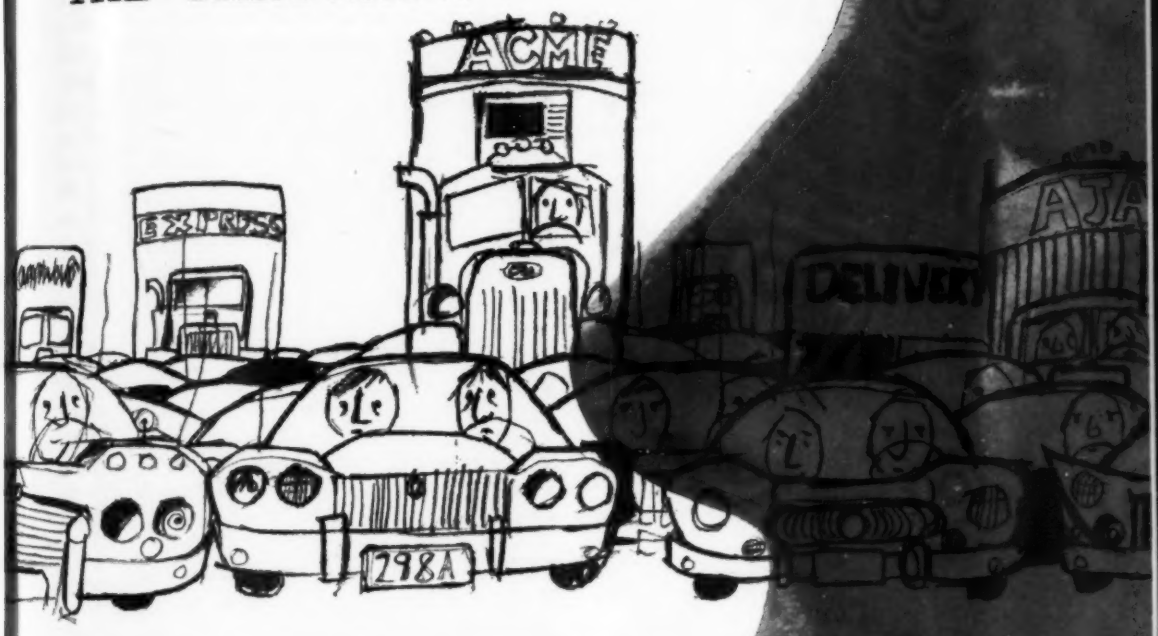

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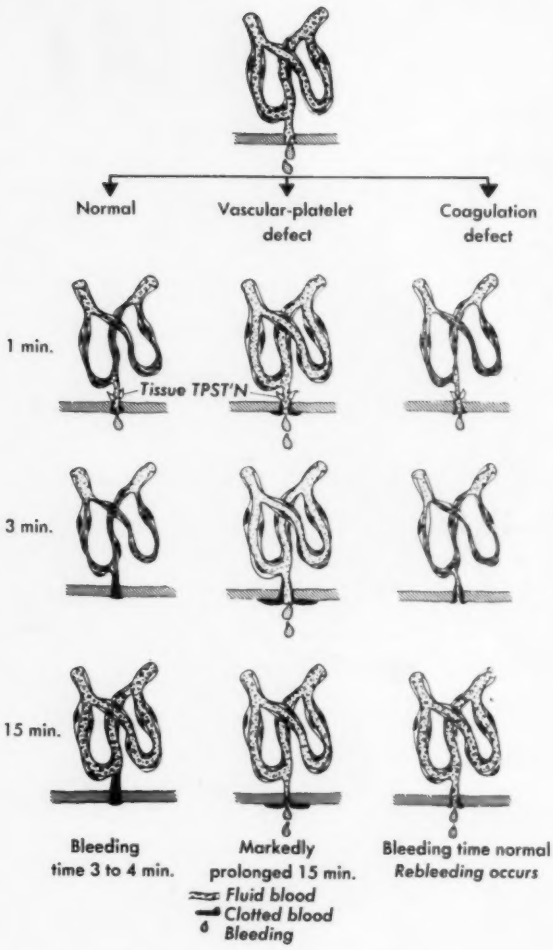

FIGURE 1. Bleeding time in hemostatic defects.

a similar result. When the defect is in the coagulation process, bleeding following trauma will be arrested during the period of vasospasm, but, when the vessel dilates, an adequate clot will not have been formed and bleeding frequently resumes. Thus, the first step in diagnosing a bleeding disorder is to determine whether it is due to a capillary-platelet defect or to a deficiency of plasma coagulation factors.

A useful test in establishing the presence of a capillary or platelet defect is determining the bleeding time, which is prolonged in this group of disorders. Two methods are available for testing the bleeding time. In the method of Duke,[1] the ear lobe is pierced with a lancet, and the drops of blood are removed with a piece of filter paper. Care is taken to touch only the drop of blood, not the ear. Normally, bleeding will be arrested and further drops cannot be blotted onto the paper after one to three minutes. In the Ivy method,[2] a blood pressure cuff is inflated to a pressure of 40 mm. of mercury; a 2 mm. incision is made on the flexor surface of the forearm with a Bard-Parker blade, and the blood is then removed with a filter paper. Normal arrest of bleeding occurs in six minutes.

Another simple but valuable test of capillary-platelet function is the Rumpel-Leede test. When the blood pressure cuff is inflated to midway between systolic and diastolic pressures and kept at this pressure for five minutes, few or no petechiae will normally be noted in the antecubital space. The presence of more than 15 petechiae in a circle 2.5 cm. in diameter just below the antecubital space is a positive result. Fortunately, few borderline results are ever obtained. If a definite platelet deficiency exists, the arm is showered with petechiae, particularly at the lower margin of the cuff and on the dorsum of the hand.

Platelets, of course, may be estimated by counting. Both direct[3] and indirect[4] methods are used. Morphologic characteristics are determined by the stained blood smear. Even in the absence of a platelet count, it is possible to estimate the number of platelets with considerable accuracy. About one platelet should be seen for every 15 to 20 red cells. When the platelet count is low it is important that the bone marrow be examined. Thrombocytopenia may be secondary to leukemia, myelofibrosis or some other myelophthisic process, and treatment must be directed to the underlying disease. In such cases megakaryocytes will be absent from the marrow, or nearly so. When megakaryocytes are present in normal or increased numbers, the thrombocytopenia is usually of the idiopathic variety. Idiopathic thrombocytopenic purpura frequently remits spontaneously. If it does not, it usually will re-

(Continued on page A-42)

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it's called the 'turista' or 'Montezuma's revenge'

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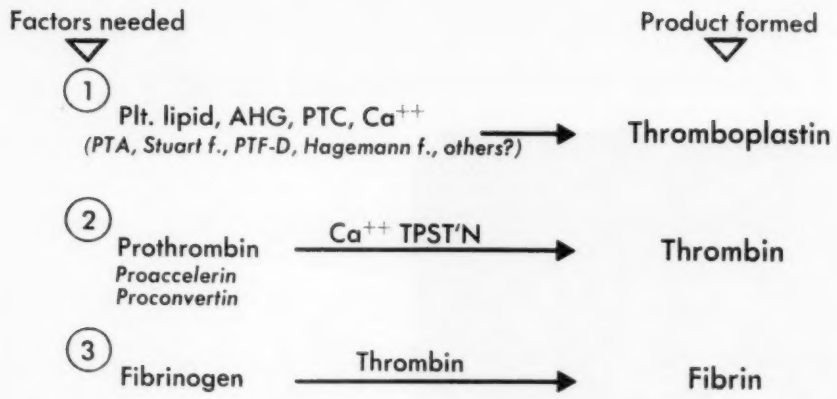

FIGURE 2. Three stages of blood coagulation. The factors listed in the left-hand column circulate in blood in an inactive form. The factors listed in the right-hand column are active coagulants, present only transiently.

spond to steroids or splenectomy or both.

Clot retraction is a function of platelets and will be absent or greatly reduced in the presence of a significant platelet reduction. Finally, the character of the bleeding is frequently an important diagnostic clue as to the underlying cause. Vascular and platelet defects are characterized primarily by petechial bleeding in the skin and bleeding from mucosal surfaces. Hemarthroses and deep hematomas are rare in such disorders.

The most fascinating group of bleeding disorders is comprised of those due to defects in the coagulation process itself. This is a field of study in which our knowledge is far from complete and in which much controversy exists. Figure 2 represents a simplification of current views on the process of coagulation.

As can be seen, coagulation is thought to occur in three stages, which may be summarized as (1) the evolution of thromboplastin, (2) the conversion of prothrombin to thrombin, and (3) the conversion of fibrinogen to fibrin. All the substances listed in the left-hand column of figure 2 are inactive in plasma and are normally present in excess amounts. The end products of each reaction are present only temporarily during the process of coagulation. Physiologic mechanisms exist for their elimination or inactivation shortly after they are formed. Thromboplastin is largely consumed during the reaction. It appears to be an unstable complex and disappears rapidly. Thrombin is in part absorbed onto the fibrin mesh which occurs in clotting and in part neutralized by powerful antithrombins. Strictly speaking, fibrin, the end product of the reaction, is not neutralized but is eventually removed by fibrinolytic ferments which dissolve most intravascular clots. Although the presence of increased amounts of these neutralizing materials can lead to a coagulation defect, this aspect of clotting is still poorly understood and will not be discussed further.

While it is clear from the preceding discussion that the blood contains an intrinsic mechanism for producing a powerful thromboplastin, many of the laboratory tests currently in use utilize an extrinsic source of thromboplastin, namely, a tissue extract of brain, lung or placenta. It is important to realize that adding such a tissue thromboplastin to a coagulating mixture completely short-cuts the first stage of coagulation and, therefore, is useful only in studying the two later stages.

The conversion of fibrinogen into fibrin is the only visible and physically measurable part of the entire system. It is, therefore, easier to discuss the problem by proceeding backward from there. Fibrinogen is converted to fibrin under the influence of a specific proteolytic enzyme, thrombin. Thrombin and fibrinogen have been isolated in highly purified forms,

(Continued on page A-44)

The effect of Unitensen (cryptenamine) on 21,913 hypertensive patients

Summary of the experiences of 2,082 physicians in private practice.
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Table 1.

No. of Patients	Results	Percent
6,822	Excellent	31.1%
11,201	Good	51.1%
2,802	Fair	12.8%
1,088	Unsatisfactory	5.0%
622	Side effects	3.0%

Basic Hypertensive Therapy

Although many of the patients in the Study also received diuretics and/or tranquilizers during the course of treatment, it was noted that the vasodilating effect of Unitensen was required to obtain optimum blood pressure control. Unitensen, a true hypotensive agent is potentiated by diuretics. A combination of the two is frequently recommended for lower dosage of each drug, minimizing the side effects of either.[1,2,3,4]

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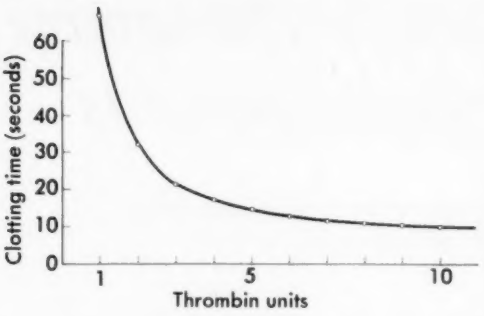

FIGURE 3. Thrombin-fibrinogen curve. This same type of curve is obtained when assaying prothrombin.

and the kinetics of their method of interaction is now well known. Thrombin affects predominantly the speed of conversion of fibrinogen into fibrin, not the amount. The concentration of fibrinogen beyond a certain minimal level has no effect on the reaction. This fact is used in measuring thrombin levels. The speed of coagulation of a fibrinogen solution or of plasma will depend entirely on the thrombin concentration added. If one relates the concentration of thrombin to the coagulation time of fibrinogen, a hyperbolic curve such as that seen in figure 3 is obtained.

The fibrinogen level in plasma normally ranges from 250 to 500 mg. per cent. This can be measured directly by converting all the fibrinogen in a small volume of plasma to fibrin by adding thrombin and then weighing the resultant fibrin. The simplest measure of fibrinogen concentration, however, is the ability of the blood to clot. In congenital afibrinogenemia, clotting does not occur on indefinite standing. Acquired cases of fibrinogenopenia occasionally occur, especially as a result of liver disease[5] or obstetric accidents.[6] In such cases a weak clot is formed which, on retraction, is unable to contain all the red cells. These fall to the bottom of the tube. Fibrinogen levels must fall below 100 mg. per cent before bleeding results. Not to be confused with fibrinogenopenia is the occurrence of a circulating fibrinolysin. In this condition clotting occurs normally, but the clot then redissolves on standing. Observation of the tube in which the coagulation time test is done will demonstrate the presence of a fibrinolysin.

If we proceed to the second stage of coagulation, the most useful test in studying this process is the Quick prothrombin time.[7] In this test, a sample of plasma (0.2 ml.) is warmed to 37° C. in a test tube; shortly thereafter equal volumes of tissue thromboplastin and calcium chloride are added. A stop watch is started at the time of the addition of the calcium chloride and stopped when the plasma coagulates. Normally, this occurs in 11 to 15 seconds. Reference to figure 2 indicates that a normal result depends on the presence of normal levels of prothrombin, proaccelerin, proconvertin and fibrinogen. A significant deficiency of any of these four factors will yield a prolonged Quick time. It is for this reason that workers in this field refer to the test result as the "Quick time" rather than the "prothrombin time." The test is not a measure of prothrombin alone, and, in many common clinical situations in which there is a prolonged Quick time, it is not the prothrombin level which is significantly diminished.

The test remains an important and useful one, however, just by virtue of its lack of specificity. Anticoagulant therapy with coumarin derivatives regularly produces a marked depression of proconvertin (factor VII, SPCA) but a much lesser depression of prothrombin.[8,9] Frequently, the depressed proconvertin levels produce the desired therapeutic effect. For the purpose of diagnosing a coagulation disorder, however, the Quick test is valuable only as a screening procedure.

In order to distinguish between deficiencies of prothrombin, proaccelerin (factor V, labile factor[10]) and proconvertin, one must be aware of certain simple differences in their properties. Both prothrombin and proaccelerin are consumed during normal clotting and are not present in serum. Proconvertin, however, is not consumed during clotting and is present in high concentration in serum. On the other hand, prothrombin and proconvertin are removed from plasma by a number of inorganic absorbents such as barium sulfate, calcium phosphate and aluminum hydroxide. On the basis of these simple facts, it is possible to

(Continued on page A-46)

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prepare (with respect to these three factors) reagents which are relatively pure. Normal serum is the source of proconvertin, and barium sulfate-adsorbed normal plasma is the source of proaccelerin. With this information, one can prepare a suitable mixture and thus narrow down the defect in a patient who has a prolonged Quick time. Thus, as shown in table 1, a plasma deficient in proconvertin will be corrected by adding normal serum but not adsorbed plasma. A plasma deficient in proaccelerin will be corrected by adding adsorbed plasma but not serum. A plasma deficient in prothrombin will not be corrected by either agent. Since all these factors are present in normal plasma, it will correct any of the three defects. In practice, this series of tests is extremely simple to perform and is done in a manner analogous to the Quick test. The test plasma is mixed with an equal volume of the corrective reagent (serum or adsorbed plasma), and equal volumes of calcium chloride and thromboplastin are added. The coagulation time with each mixture is noted, and the diagnosis is then relatively simple.

There have been numerous reports of congenital deficiencies of proaccelerin and proconvertin. A pure congenital deficiency of prothrombin has not as yet been found, and, in fact, only a single case of acquired pure prothrombin deficiency is known in the world literature.[11] Acquired types of defects include deficiencies of all these factors, the best known being the double deficiency of proconvertin and prothrombin induced by coumarin drugs[12] and also seen in obstructive jaundice and hemorrhagic disease of the newborn.[13] Hepatocellular liver disease also produces depressions in these blood coagulation factors, and it is now fairly well established that the liver is the main source of synthesis of these proteins.[14] Since prothrombin is quantitatively converted to thrombin by the action of thromboplastin, the quantitative measurement of prothrombin levels is determined by the shape of the thrombin-fibrinogen curve shown in figure 3. In fact, the standard prothrombin dilution curve differs from the curve shown in figure 3 only in that thrombin units are expressed in terms of prothrombin per cent of normal.

TABLE 1

DIAGNOSING DEFICIENCY IN SECOND STAGE OF COAGULATION

DEFICIENT FACTOR	QUICK TIME CORRECTED BY:		
	Serum	*Adsorbed plasma*	*Normal plasma*
Proconvertin	Yes	No	Yes
Proaccelerin	No	Yes	Yes
Prothrombin	No	No	Yes

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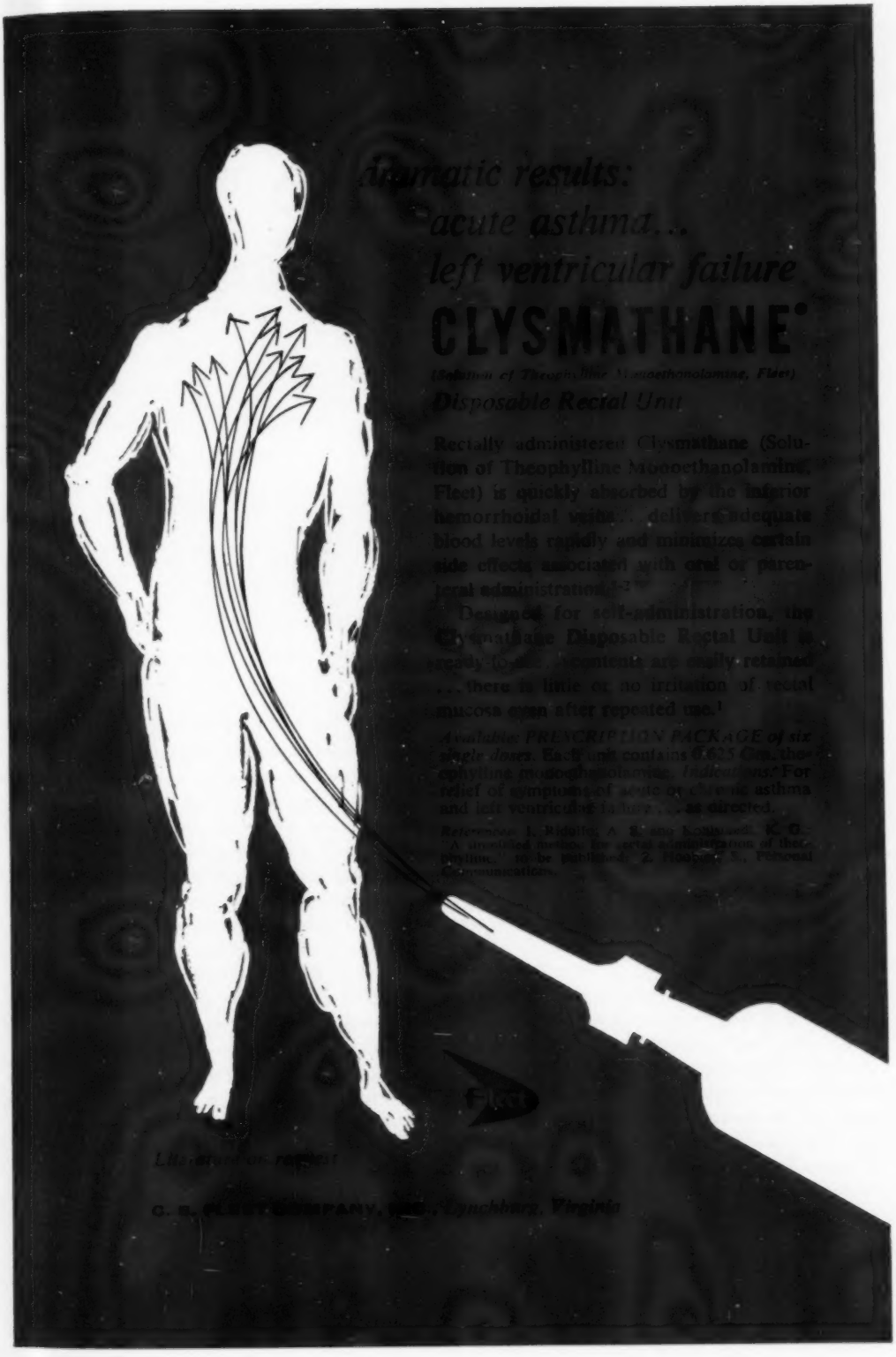
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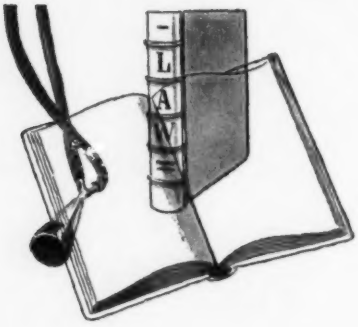

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Western Reserve University, Cleveland

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Achievements of Law

Western law has provided a great measure of peace and order within the communities of men. In the five centuries since the beginning of world exploration, wildernesses have been transformed to frontiers and frontiers to communities. Western law governs much of this world territory today. The significance of Western legal concepts was forcibly demonstrated when the sovereign nation of India was established only a decade ago. This predominantly Hindu civilization accepted the basic English common-law system of justice. The experience of India as a colony under the common law had been so fruitful that English law remained after the Englishman retired.

Our law has provided a second enriching spirit as it has pursued truth—human rights. The foremost achievements in this pursuit are the English parliamentary enactments of the seventeenth century, the American Declaration of Independence, and the French Declaration of the Rights of Man in the eighteenth century. Our generation has witnessed one fruition of this pursuit in the United Nations' Universal Declaration of Human Rights and the International Covenants on Human Rights.

Today, Western law pursues a third great concept—equality. Problems of law encompassing racial, religious and ethnic equality predominate in our world community and are demonstrated by the desegregation of public schools in Little Rock and of white housing neighborhoods in Cleveland, an apartheid program in South Africa, and liquidation of the Baltic peoples in Soviet Russia. Much unfin-

(Continued on page A-54)

*Professor of Law and Director, The Law-Medicine Center, Western Reserve University, Cleveland, Ohio.

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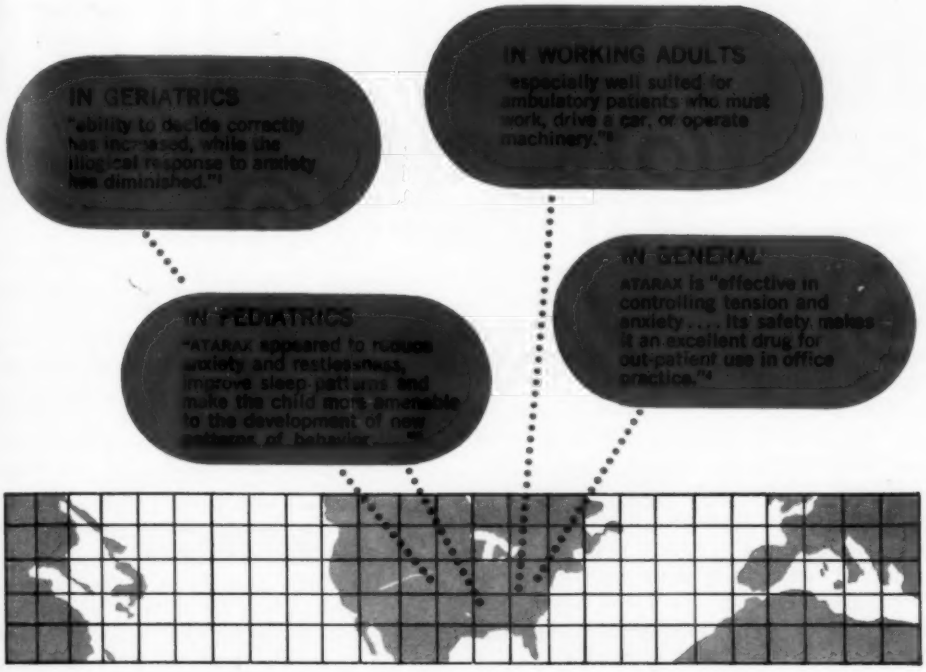
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ished business confronts Western law as it seeks to establish equality.

No one has summarized law's pursuits of these truths—peace and order, human rights and equality—more eloquently than did Thomas Jefferson in writing the Declaration of Independence:

> We hold these truths to be self-evident, that all men are created equal, that they are endowed by their Creator with certain unalienable Rights, that among these are Life, Liberty and the pursuit of Happiness. That to secure these rights, Governments are instituted among Men, deriving their just powers from the consent of the governed.

Achievements of Medicine

What has been the history of Western medicine as it has pursued truth through the ages? Centuries ago, life expectancy was 30 years; today, it remains the same in lands not enriched by Western medicine. Where Western medicine prevails, the life span is now 70 years and is still climbing. Today, plagues have been conquered, disease germs greatly vanquished, viruses vigorously attacked. Understanding of the chemistry of both body and mind has opened the widest vistas. Surgery repairs the human body in ways not even conceived several decades ago; blood banks, skin banks, bone banks and eye banks have been instituted. Preventive medicine also has crossed the threshold on a broad front. "The conquest of enduring health is near at hand," one observer declared; or, as Bertrand Russell stated:

> The world is moving into a happier era than it has ever known. Mankind cannot long continue to preserve any degree of sanity or balance unless it can find a way to diminish nervous stress. The world has begun to go rather slowly and rather tentatively toward life, as opposed to death.

Medicine in the West now can become primarily concerned with life instead of with the age-old challenge of death. Its pursuit of truth has borne ripe fruits: an increased life span; control of man's twin miseries, disease and injury; prevention of disease and injury, or, better yet, preservation of a state of good health for body and mind.

Common Goals

From this historical record, practicing attorneys and physicians can readily discern a common unity in their respective professions—the pursuit of truth. Other rich concepts unite our professions, such as the emerging belief that both lawyer and doctor must serve the whole man; whether he is a client or patient, he is, foremost, a human being.

Law encompasses more than technical rules of behavior; it threads endlessly through all man's experiences. At the dedication of the American Bar Center in Chicago in 1953, Justice Robert H. Jackson[1] of the United States Supreme Court observed:

> Law is not government nor is it politics, though it is closely related to political science and receives particular "positive" rules from legislation. Our law is not religion, although many of its finest precepts are drawn from religious teachings. Law is not economics, though it is deeply involved with economic problems; nor is it sociology, though its chief concern is with the welfare, health and well-being of society.

Zilboorg[2] similarly recognized medicine's concern with the whole man:

> The history of medicine, in the true sense of the words, is not the history of medical discoveries only; nor is it of course the accumulation of the biographies of great medical personalities. All these things are only a part of the history of medicine, as the history of wars and the list of presidents and kings are only a part of general history. The history of medicine is really a complex synthesis of man's life through the ages, in sickness and in health, in peace and in war, in living and in dying—man as a patient whose suffering is to be alleviated, man as a poor wretch who cannot pay for his health and who pays for life with disease, man as a victim of the carelessness of the community as a whole, man as a part of the community which looks after the health of the great and the small. In other words, the history of medicine involves the history of the economic, social, intellectual and cultural life of man. It is also the history of the doctor's functions as a healer who, while economically dependent on the patient, must yet remain in-

(Continued on page A-56)

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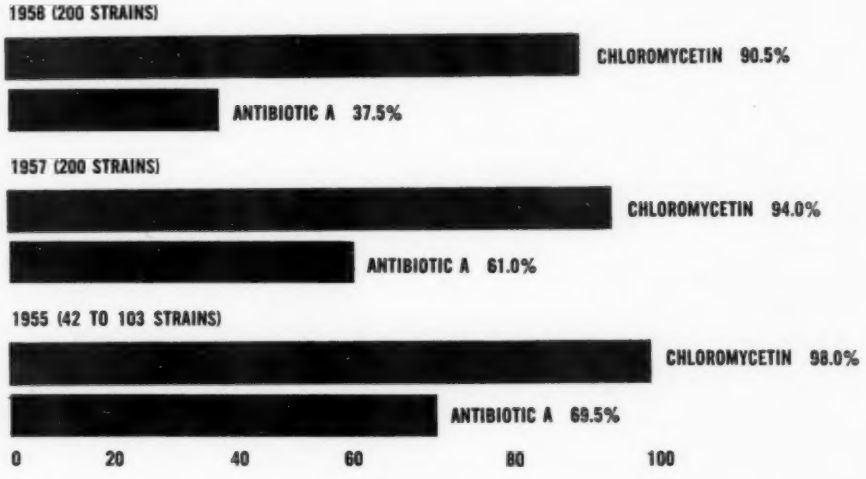

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dependent, in some transcendental way, of all economic motives—which is, of course, impossible. It is also the history of the doctor's sense of responsibility toward the underprivileged and the social derelicts. In short, it is the human being with all his frailties and prejudices—economic, social, racial. It is the history of the cultural atmosphere in which medicine has bathed, or has been stifled, or has lived throughout the ages.

Despite our common need to serve primarily the human being and secondarily the client or patient, too many of us forget this whole human entity.

In delivering the 1958 George W. Gay Lecture on Medical Ethics at Harvard Medical School, Justice Felix Frankfurter,[3] United States Supreme Court, listed three shortcomings of lawyers: They pursue their calling too narrowly; they live too exclusively within the profession; and they do not cultivate enough intellectual detachment. He then stated: "I leave you to decide to what extent they (these shortcomings) apply to doctors." Justice Frankfurter concluded the lecture by warning that "specialization is the 'mutilization' of the whole."

Our professions have a common ideal: to serve man as a whole. In practice these professions have become slaves to specialization. Today, we need more than specialized practitioners; the development of *civilized* practitioners is imperative.

Divisive Factors

If fidelity to the pursuit of truth and dedication to the service of the whole man are uniting ties which bind attorneys and physicians in a common understanding, what elements divide us?

It is unfortunate enough when we take the whole man and specialize on him as a client or patient; but when this whole man becomes simultaneously a client and patient—a human being with both medical and legal problems arising from the same experience—our professions commonly become not merely specializing practices but actually participants in open warfare against each other. If specialization mutilates the whole being, our professional warfare desecrates him. Doctors often refuse or are most reluctant to become expert medical witnesses in the administration of justice. Lawyers interested only in legal rights may prolong legal cases, destroying medical therapy which seeks to restore the client rapidly as a whole man with good health. Here are but two crucial examples of the vital practical challenges to our professions as they seek to serve the whole human being.

But this open warfare which permeates our bar association meetings and our medical society assemblies or spews vulgarly over onto the pages of daily newspapers represents only the *symptom*. The *causes* should concern us. Then the *cures* can be effected.

I believe that there are four major differences between law and medicine. Obviously they are not exclusive; they may even be incorrect. At least they represent one lawyer's beliefs after considerable experience with a law-medicine program.

In simple terms these four differences are in (1) the purposes of our professions, (2) our relations to the persons we serve—clients or patients, (3) the semantics in our practices, and (4) the rate of advancement of our individual professions. In all four categories the differences are both broad and deep.

Purposes—The purpose of medicine is to maintain the patient in the best health, to overcome his disease and injury, and to lengthen his life span. The purpose of law is to maintain peace and order in the community of men, to respect the human personality of clients through human rights, and to provide equality of opportunity. To achieve these purposes medicine emerges from the laboratory by the scientific process; law emerges from the community by the process of experience. People follow medicine; law follows people.

As individuals, we often accept new preventive, diagnostic and therapeutic medical practices with complete reliance on and faith in medical scientists alone. However, as a community of men, we often refuse to accept new legal rules of conduct for self-government rendered in the administration of justice. Witness the reluctance to desegregate public schools in the South or white housing in

(Continued on page A-58)

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neighborhoods in the North. We need community mores, experiences, customs and culture to undergird law; otherwise, law will not achieve its purposes of peace and order, human rights, and equality of opportunity in a community. We need only laboratory and scientific experience to respond to medicine's purposes of maintaining good health, overcoming disease and injury, and lengthening life. The purposes of law and medicine truly differ. These differences stimulate two different responses in people: They will follow medicine but they must lead law.

Relationship to client or patient—A second factor separating law and medicine is the relationship between the practitioner and the person he serves—client or patient. Doctor-patient relationship demands that the patient place himself in the doctor's care. The doctor in turn commands the patient without outside interference from other human beings. The doctor-patient team fights nature—disease, injury and death.

The lawyer-client relationship requires that the client place himself in the lawyer's control. Although the lawyer commands the client, he must consider external human influence, such as the other party to the legal conflict. The lawyer-client team clashes with another human being or human institution. These opposing individuals or institutions have legal rights, too. In its basic purpose, law is concerned with this clash between two human personalities. Law must accommodate and settle these human differences if it is to achieve its purposes of peace and order, human dignity and equality. Medicine must accommodate and settle the differences between one human being and nature if it is to achieve its purposes of longer life, curing disease and injury, and maintaining good health. The medical practitioner serves one human being influenced by nature. The lawyer performs the same service, but the influence of another human being is paramount. In serving their fellow men, lawyers and doctors provide completely different services.

Semantics—The semantics of our two professions probably provide the most divisive element between us. Consider one word used freely in both practices—"cause." Each profession uses the same word, but each ascribes to it a different meaning. For example, the doctor often states that a certain factor causes the patient's ill health if it is 25 per cent responsible. This factor must be handled medically if the patient is to recover full health, even though other factors also contribute to the ill health. In its resolution of human conflicts the law requires that the causal factor be at least 51 per cent responsible; 25 per cent is not enough. Or, as the judge will charge the jury in a personal injury case: "If you find by the preponderance of the evidence, which means the greater weight of the evidence, that the plaintiff's physical condition was caused by the accident, you shall find for the plaintiff."

Words separate people. When they signify different meanings, even the same words may create discord.

Rate of advancement—The fourth dividing element between the professions is the speed with which medicine and law advance. Since medicine leads people, it is not primarily harnessed to community mores, customs, experiences and culture. Scientific minds imagine; medical laboratories probe; doctors experiment; dramatic triumphs in better health are achieved. Since the people lead the law, the law is primarily fettered to community mores, customs, experience and culture. Legal minds search for precedents, accept *stare decisis*, appeal to the jurors' common knowledge and beliefs, and obtain decisions compatible with the community mores.

An interesting illustration of this dividing element is found in blood grouping. We have known for some decades that scientific blood grouping can exclude a man as the father of a certain child. Medicine accepted this fact immediately after scientific experiments proved it; however, the law has been slow to accept it in administering justice. Last year in Ohio, a significant case emphasized the problem. In Cuyahoga County Juvenile Court, a mother complainant sought to establish the male defendant as the father. A jury trial was waived. The judge heard the case and graphically sketched the issue:[4]

(Continued on page A-60)

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The burden of proof was on the complainant to make out her complaint and charge by a preponderance of the evidence. These are the factors preponderating in favor of the complainant: her own and her mother's unrebutted testimony, the child being exhibited to the court for the purpose of showing physical resemblance to defendant; refusal of defendant to submit to cross-examination on constitutional grounds; and his failure to testify on his own behalf.

Giving full weight to all these factors, has the complainant succeeded in proving the guilt of the defendant by a preponderance of the evidence—notwithstanding the testimony of the expert serologist that the blood-grouping tests establish the exclusion of the defendant as the father of the child?

The court then acknowledged the wide disparity in the speed of progress between medicine and law:[5]

It is apparent that in Ohio, legislative law has moved more slowly than scientific research in giving full weight to blood-grouping tests which definitely exclude paternity.

Finally, because community mores, customs, experience and culture now recognize the value of scientific blood grouping, the following decision could be rendered:[6]

But this court cannot close its mind to the great advances in the science of blood-grouping tests since 1939, and to the modern recognition by medicolegal resources of the high value of such blood tests as a wholesome aid in a quest for truth in the administration of justice in matters relating to contested paternity. This court further believes that the near unanimity of medical and legal authorities on the question of the reliability of blood-grouping tests as an indicator of the truth in questioned paternity cases justifies the taking of judicial notice of the general recognition of the accuracy and value of the tests when properly performed by persons skilled in conducting them. The law does not hesitate to adopt scientific aids to the discovery of the truth which have achieved such recognition.

This court has the duty to determine if the conditions exist which made the biological law operative. That is to say, were these tests properly made, and are the results as reported free from error? If so, the exclusion of the defendant as the father must follow irresistibly. Enlightened judicial acceptance of the verdict of science must result in the conclusion that where blood-grouping tests in a bastardy proceeding prove nonpaternity this court is not warranted in closing its mind to the conclusion which science declares is established—unless there is proof that the tests were not properly made or that conditions did not exist to make the biological law operative.

Doctors who witness speedy progress in medicine often have great difficulty in comprehending the slow progress of law. Lawyers experience the opposite difficulty.

Uniting Law and Medicine

Must we accept these four suggested dividing elements as inevitably insoluble? Can we construct bridges between the professions? Will anyone deny that the progress of Western man has been achieved by just this procedure, i.e., building bridges across the depths of human ignorance? Our task in law and medicine should not prove so difficult, for we will be building a bridge to unite two ancient, learned professions. We need not construct into the dark unknown. How shall we proceed?

Our blueprint for the bridge must be *understanding*. First, we must understand what unifies our two professions. Both are ancient and learned practices; both pursue truth, and both are dedicated to serve our fellow men. Next, we must understand what elements divide us: the differences in our purposes, our relations with those we serve, our semantics, and the speed of our advances. We must emphasize *understanding* the differences, not *resolving* them. We shall not make lawyers in the image of doctors, nor doctors, lawyers. To attempt to resolve these differences would be to depreciate both professions. To understand these differences would be to give strength to both professions.

Our tool to construct the bridge is the use of medicine as a major source of truth in the administration of justice. Since the prime purposes of law are to effect peace and order, undergird human rights, and establish equality, the role of law must be to settle human conflicts. In our system of jurisprudence these conflicts are settled by applying just laws to

(Continued on page A-62)

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truthful facts. Much litigation today involves medical issues. Medicine must be used to provide truthful medical facts and opinions to settle or adjudicate legal conflicts. This tool demands constant sharpening if our bridge is to be built to endure.

Once constructed, a bridge is of no value unless people cross it. Physicians must cross to the law side by accepting the responsibility to provide truthful medical facts and opinions in the administration of justice. This can mean the willingness to be a witness for the client-patient. Lawyers must cross to the medicine side to aid in the doctor's preventive, diagnostic and therapeutic tasks. This can mean resolving the legal conflict speedily in order to permit the best medical recovery of the patient-client.

A blueprint, a tool and the traffic on any bridge first require engineering. Our educational institutions play this role. Schools of medicine and law must assume obligations to educate their students on the problems here presented. Since education is an unending process, let our professional societies also be concerned with bridging this chasm of professional ignorance. Education may take the form of instruction, research or publication. Each has its special function. After all, both professions are learned societies. Has not education within our individual groups been a dominant force in making them learned?

We have the opportunity and privilege to become civilized citizens, not merely specialized practitioners. In so doing we would best serve not only the individual whole man, the client-patient, but also the Western civilization which has blessed us with citizenship.

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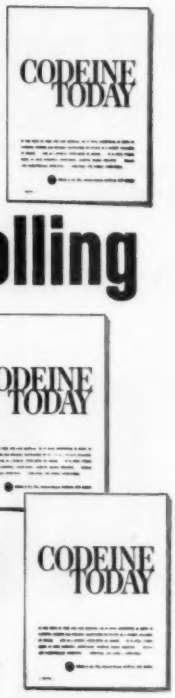

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Intestinal Obstruction

PAUL C. HODGES*

For most x-ray examinations of the alimentary tract one employs suspensions of barium sulfate, administered by mouth or by rectum, but usually no artificial contrast medium is used for examinations of patients suspected of having intestinal obstruction. When, by means presently to be described, one has made a tentative diagnosis of partial or total obstruction of the colon, it is both permissible and advisable to continue the examination by fluoroscoping and filming the colon during the administration of a barium enema, taking care to avoid forcing any of the barium beyond the point of obstruction. Barium administered orally or by enema and introduced proximal to an obstruction in the colon is apt to impact, rendering a partial obstruction complete and seriously complicating the preoperative preparation of the patient. Orally administered barium is much less likely to impact in the small bowel, but usually the diagnosis of bowel obstruction can be made without it and, as a matter of fact, it seldom is used.

I shall discuss simple acute mechanical obstruction of the jejunum, ileum or colon diagnosed from abdominal films made without the aid of artificial contrast media. I will leave for the monographs or for possible subsequent consideration here such important but involved matters as closed-loop obstruction, functional paralytic or adynamic ileus, incomplete obstruction, intermittent obstruction, occlusion of the blood supply of an obstructed loop, and peritonitis complicating intestinal obstruction. Furthermore, I shall avoid the temptation to discuss the origins, permutations and ambiguities of the term "ileus," sticking to the simpler and less controversial "obstruction."

*Emeritus Professor and Chairman, Department of Radiology, University of Chicago, Chicago, Illinois.

Gas in Bowel

There is wide individual variation in the amount of air normally present in the alimentary tract. Nursing children usually and normal ambulatory adults occasionally harbor large amounts of air in the colon. Adults who when ambulatory and in good health have very little intestinal air (figure 1) may accumulate much more during attacks of functional bowel distress or following confinement to bed because of injuries or disease, even of an extra-abdominal nature (figure 2). In such cases there may be pain, vomiting and considerable abdominal

FIGURE 1. Normal ambulatory adult. An active 47 year old man was examined because of low back pain. There is only a very small amount of air in the ascending, transverse, descending and sigmoid portions of the colon, and none in the small bowel.

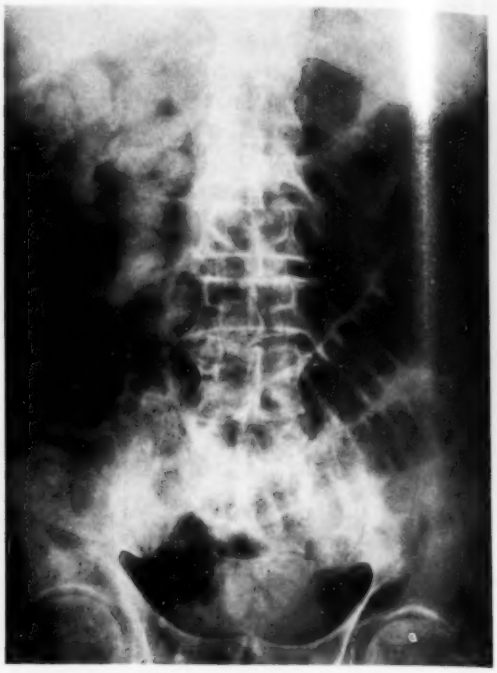

FIGURE 2. Bedridden peptic ulcer patient. A 77 year old man had been under treatment for many years for peptic ulcer. At the time of this filming he had been in bed for some days, receiving antacid therapy. Fecal impactions had developed and subsequently were relieved without recourse to operation. Presumably the ileocecal valve was incompetent, allowing air to back up into small bowel loops, which can be seen in the lower left quadrant.

distention, but the continued passage by rectum of gas and even some feces argues against obstruction. Radiologic demonstration that the gaseous distention involves almost the entire alimentary tract from stomach to rectal ampulla provides further negative evidence.

When the bowel is mechanically obstructed by a band of adhesions, volvulus, intussusception, a large gallstone, a mass of *Ascaris* worms, or an unreduced hernia, etc., the clinical evidence is not always conclusive, particularly during the period that the patient is emptying the colon below the point of obstruction. X-ray films interpreted with careful reference to the known clinical facts may be of the greatest importance in establishing the correct diagnosis. When an obstruction halts the forward movement of intestinal content, and air and fluid continue to be introduced from above, the bowel proximal to the obstruction becomes distended with fluid and air, whereas that distal to the obstruction eventually empties (figure 3). In most cases the radiologist not only can establish that there is an obstruction present but also can give the approximate anatomic location of the obstructing lesion. In order to do this, he must have the assurance that attempts are not still being made to administer cleansing enemas with the possible introduction of air through the enema tube into the bowel distal to the point of the obstruction.

X-ray Appearance of Jejunum, Ileum and Colon

Anatomically, proximal jejunum has a thicker wall, a larger caliber, and better-de-

FIGURE 3. Mechanical obstruction of proximal ileum. A 69 year old man had a 36 hour history of cramping lower abdominal pain, with nausea and no stool. There was tenderness in the left lower quadrant and active peristalsis could be seen. Film shows distended small bowel loops arranged transversely in the so-called ladder pattern, with plicae of adjacent loops forming the so-called herringbone pattern. The colon and distal small bowel are empty and, therefore, radiologically invisible.

At operation, a loop of proximal ileum was found herniated into a defect in the sigmoid reflection. Its blood supply was intact and the patient recovered following reduction of the hernia and repair of the defect.

NOTE: The bag of the Miller-Abbott tube has ruptured, allowing metallic mercury to outline some of the loops of small bowel.

FIGURE 4. Obstruction low in the colon by volvulus of sigmoid. A 66 year old woman had a two day history of distention, right-sided abdominal pain and vomiting. Film shows enormous distention of bowel loop interpreted as sigmoid and subsequently identified as such by barium enema and surgery. In the upper right quadrant lies less distended and more normal-appearing transverse colon.

Under fluoroscopic control it was possible to partly decompress the sigmoid loop by means of a tube introduced through the rectum. At surgery the entire colon was abnormally mobile, the sigmoid twisted on its mesentery and gangrenous. The gangrenous portion was successfully resected.

This case illustrates the fact that when colon loops are sufficiently distended they may be pushed into the central portion of the abdomen, where ordinarily one expects to find small bowel.

veloped plicae circulares than distal ileum, but distal jejunum passes insensibly into proximal ileum with only convention and no organic change at the point of transition. The entire small bowel is gathered onto a mesenteric root that is approximately 7 in. long and is attached to the posterior abdominal wall along a line that starts above at the left side of the body of the second lumbar vertebra and passes obliquely downward and to the right to terminate in the right iliac fossa. The entire small bowel, therefore, is located in the central portion of the abdomen, with jejunum in the upper left and ileum in the lower right and with individual loops of bowel arranged approximately at right angles to the long axis of the body. The colon, of course, is of much larger caliber with its haustra much larger than the spaces between the plicae circulares of the small bowel and with its location in general peripheral to the small bowel.

Colon Obstruction

In most patients the ileocecal valve is sufficiently competent to prevent the backflow of air and fluid from colon into small bowel. In

FIGURE 5. Obstruction of terminal ileum by adhesions to anterior abdominal wall. A 78 year old man had been vomiting fecal matter for one week before admission. Film shows gas-distended loops of small bowel with no air in colon. At operation immediately following filming, the terminal ileum was found to be necrotic, perforated and adherent to the anterior abdominal wall. Purulent peritonitis was present. Local resection was done but patient died five hours following operation.

In retrospect, the "spine" of the herringbone pattern in the lower left quadrant is broader than usual, suggesting that the adjacent walls of bowel loops which form the spine pattern are thickened by peritonitis. This phenomenon is known to occur but findings are difficult to interpret and there are numerous errors of omission and commission.

such patients mechanical obstruction in the colon produces an empty colon below the point of obstruction and a gas-distended colon above the obstruction, but no gaseous distention of the small bowel for at least a considerable number of hours after the onset of obstruction. When distention becomes severe, the haustral pattern may be lost and distended redundant loops may be pushed centrally away from their normal peripheral location in the abdomen (figure 4).

Small Bowel Obstruction

Three clichés which had best be disposed of at this point are: (1) the herringbone pattern, (2) the ladder-rung pattern, and (3) fluid levels.

When loops of small bowel—particularly jejunum and proximal ileum—are moderately distended with gas, the plicae circulares stand out as white bands silhouetted against the black bands representing air between the plicae; and when two distended loops lie adjacent to one another, the apposed walls of these adjacent loops show as a single white longitudinal line lying at approximately right angles to the images of the plicae. Some early worker thought that the pattern looked like the well-picked skeleton of a herring with the two bowel walls representing the "spine" and the plicae of adjacent loops representing the "ribs" of the fish (figure 5). Perhaps it was the same worker who, noting that distended loops of small bowel tend to arrange themselves one above the other transversely across the center of the abdomen, thought that they resembled the rungs of a ladder. These metaphors reflect the thinking of a period when radiologists considered it presumptuous to speak of seeing this or that tissue or this or that lesion, and felt that the most they could do was to describe shadows.

When any hollow viscus or other space within the body contains a mixture of air and fluid, and when patient and beam of radiation are arranged so that the beam is tangential to the interface between air and fluid, a fluid level will be seen. Sometimes (as in the case of the maxillary sinuses) the presence of fluid can be detected only by tangential films; this is usually the case in lung abscess with bronchial fistula. Almost inevitably the small bowel and proximal colon contain fluid, and if they also contain air there will, of course, be fluid levels if the radiation is directed tangential to the interface. Here, however, it is seldom that tangential views are required to establish the fact of gaseous distention. The most important

exception is in closed-loop obstruction where the air content may be so small that it will be missed in the absence of tangential films.

In conducting an x-ray examination on a patient suspected of having intestinal obstruction, it is essential to obtain films of the best possible technical quality; usually these are best made with the patient recumbent and immobilized with a compression band. If his condition permits his standing or sitting for additional tangential films, or if it is feasible to obtain tangential films as he lies on the table, such films may be of genuine ancillary value; but it is a serious mistake to exhaust the patient by having him stand or sit for such films and then fail to get high-quality films in the recumbent position.

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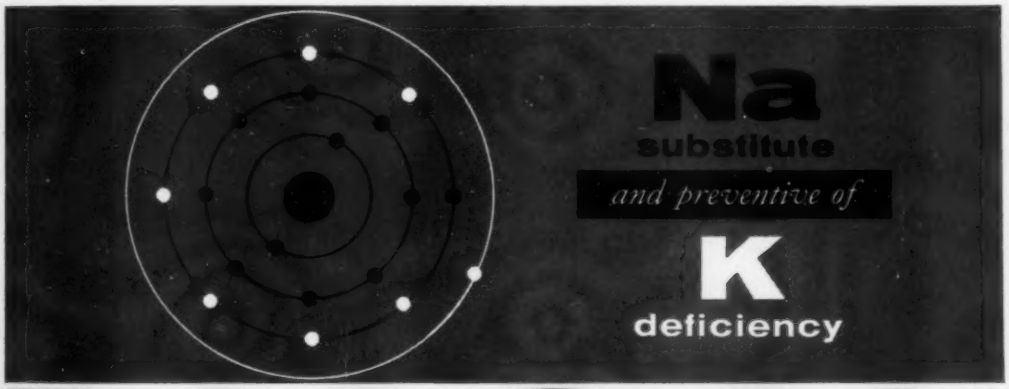

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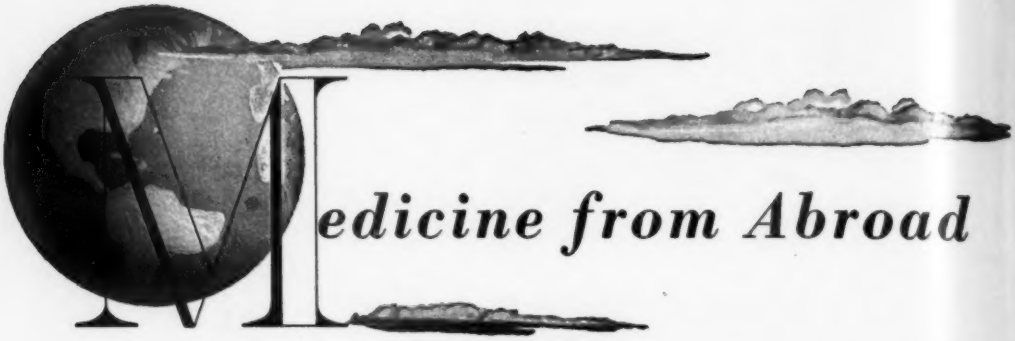

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FROM POSTGRADUATE MEDICINE'S CORRESPONDENTS

AUSTRIA

Diaphragmatic hernia—At a scientific session of the Viennese Pediatric Society, Drs. H. H. Jenny and F. C. Havranek discussed the diagnosis and surgical treatment of diaphragmatic hernia. They presented three cases to illustrate possible complications and diagnostic difficulties in this condition.

A girl aged three years and nine months had an incarcerated diaphragmatic hernia on the right side; it passed through the diaphragm laterally from the inferior vena cava, partially displacing the stomach into the thoracic cavity. The chief symptoms were vomiting, acetone in the urine, and dehydration. Surgical intervention by laparotomy produced good results.

The second patient was a seven month old girl who had vomited frequently since birth. This condition had been misinterpreted as habitual vomiting. When admitted to the hospital, the patient had varying symptoms of obstruction. A successful operation through the chest revealed a parahiatal hernia. The stomach was replaced from the left thoracic cavity to its normal position in the abdominal cavity.

The third patient described was a 17 month old girl who had a congenital defect of the diaphragm in the region of the foramen of Bochdalek. Inflammation of the bronchioles resulted in both emphysema and bilateral tension pneumothorax. The right side was drained by Bülau's method, but the child died due to detachment of the lower mediastinum from the spine and of the descending mesocolon from the retroperitoneal tissue, which caused fatal bleeding into the peritoneal cavity.

Although the hernias in these patients differed in regard to their abnormal rings and contents, each patient became suddenly ill and had life-endangering complications. After such complications appear the operative risk is considerably greater. By means of additional case histories and roentgenograms, Drs. Jenny and Havranek demonstrated the difficulties of detecting diaphragmatic hernias. Even in cases of total eventration it cannot be definitely determined that the diaphragm is completely missing, since the eventration may be caused by small ruptures of the Larrey or Bochdalek type.

Although no symptoms may be evident, a congenital diaphragmatic hernia should be surgically treated. The operative risk is not as great today as formerly, and children with these hernias constantly face the danger of fatal illness. Dr. Jenny reported one death in nine patients who had had operations. The only exception to surgical treatment is the case of a sliding hernia in which a portion of the gastric fundus is pushed upward through the esophageal hiatus. In such cases, the hernia should be operated on only after conservative treatment has failed or on appearance of esophageal stricture and ulcerations which hinder normal feeding of the child.

Dr. H. H. G. Wolf called attention to use of

(Continued on page A-86)

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WALLACE LABORATORIES, *New Brunswick, N. J.*

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artificial pneumoperitoneum for analyzing questionable radiopaque densities, the same procedure used for analyzing diaphragmatic humps of the liver. Dr. Jenny has used pneumoperitoneum in adults but not in children. It is difficult to decide whether a prolapse or a hernia is present if the peritoneum is not visible.

Dr. H. P. Salzer mentioned that for large eventration hernias in the newborn he performs an abdominal operation, since a patient died of chronic intestinal obstruction after he used a transthoracic intervention. Drs. Jenny and Havranek believe that transthoracic incisions should be used in all operations on acquired or traumatic hernias or prolapses. In these cases adhesions between the prolapsed intestines and the lungs may be expected, and they cannot be reached through a laparotomy.

BRAZIL

Hyperostosis frontalis interna—In the *Arquivos dos Hospitais da Santa Casa de São Paulo*, Ulisses Lemos Torres, José Alve Brandão and João Elias stated that nothing is known positively about the pathogenesis of hyperostosis frontalis interna (HFI).

The authors analyzed 17 cases of HFI selected from 5000 observations recorded in the outpatient endocrinology department of the Municipal Hospital at São Paulo. In 85 of 680 patients who had been x-rayed for reasons such as headache, obesity, acromegaly and virilism, the diagnosis was hyperostosis; in 17 patients, all of them women, the diagnosis was HFI.

These 17 women were measured according to Viola's and Sheldon's methods, and detailed studies of age, nutritional status, headaches, psychic disposition, menses, hormonal and biochemical assays and somatotypes were made. The only deviation revealed by urine, blood and other laboratory tests was a slightly decreased calcium content in some patients. The obesity in 12 of the 17 patients was of the usual type, without abnormal fat, and the hypertension was benign (Volhard's red type). The menstrual disorders and the neurophysiologic features bore no relation to the hyperostosis.

Because the symptoms were extremely varied and showed no proportion to the HFI, a cause-effect correlation could not be discerned.

The authors were able to establish two clinical types: the classic and the x-ray. The classic type showed, in accordance with Morgagni's description, a dysplastic constitution, obesity and virile appearance, associated with hirsutism, hypertension or psychic disturbances. In the x-ray type, hyperostosis was the principal manifestation, without the classic somatotype of Morgagni's syndrome, although some of the symptoms usually found in the syndrome were seen.

Morgagni's syndrome, in the authors' opinion, is characterized by benign hypertension and a paramorphic, dysplastic constitution, bordering on the pathologic. Frequent disturbances of the pressure regulation and of glycosides are observed. If the hirsutism and intolerance to hydrocarbonates are considered, this syndrome resembles that of adrenal hypercortical obesity or Achard-Thiers diabetes. Of the symptoms ascribed to the syndrome, the megalosplanchnic somatotype was the one most often found in the 17 patients studied.

The authors have concluded that the symptoms they noted do not refer to the hyperostosis, but to a hormonal-chemical correlation due to the short megalosplanchnic somatotype, which corresponds to Kretschmer's hyperplastic type. This syndrome occurs most frequently in women because of their hormonal make-up. According to the authors, hyperostosis frontalis interna is yet another manifestation of the megalosplanchnic somatotype.

In order to demonstrate their thesis, the authors made a clinical study of the symptoms of short megalosplanchnic and dysplastic patients whose x-rays did not indicate hyperostosis. They noted bone changes indicating that these patients had tendencies to excessive deposition of calcium in the cranial bones. Since Morgagni's symptoms were found as often as the bone changes, the authors considered both conditions to be expressions of a single status which, because of its polymorphic manifestations, has been interpreted in various ways.

In determining the pathogenesis of HFI, the metabolic theory could not be demonstrated. As for the endocrine theory, although there were various endocrine disorders, such as toxic goiter, Basedow's disease, diabetes mellitus, and hypophysial atrophy due to compressions, no single condition was definitely prevalent.

In their summary the authors stated that hyperostosis frontalis interna seems to be an effect, not a cause. Morgagni's classic syndrome describes changes frequently seen in short megalo-

(Continued on page A-88)

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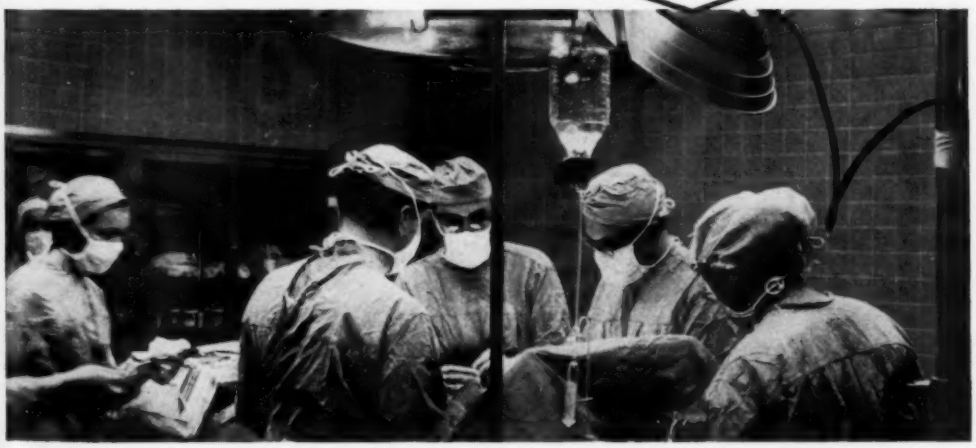

splanchnic dysplastic body types. These changes include obesity, benign hypertension, decreased tolerance to hydrocarbonates, anxiousness, and, rarely, a tendency to bone deposition which is expressed in the x-ray features of hyperostosis frontalis interna.

ENGLAND

Centenary of the General Medical Council—Even today it is not illegal in England to practice medicine without a license or indeed without training. Herbalists and bonesetters still flourish in rural districts, and chiropractors and osteopaths in the cities. However, giving a death certificate, giving medical evidence in the law courts, treating venereal disease, or serving as a medical officer in the armed forces is forbidden to those not qualified. The practice of medicine and surgery had been regulated by a variety of statutes dating from the reign of Henry VIII; nevertheless, in 1858, when the General Medical Council was set up, 5000 of the 15,000 persons then practicing medicine in England were quacks.

In 1815, an act was passed which allowed apothecaries to practice medicine (formerly prevented by the corporations of physicians and surgeons), and in 1832 they banded themselves together to form the British Medical Association. One of the first endeavors of the B.M.A. was to reform the medical profession by purging it of untrained quacks and to allow practice everywhere by trained medical practitioners wherever they might have qualified; but vested interests, including the universities, and Royal Colleges of Physicians and of Surgeons, obstructed the efforts of the reformers until 1858. The General Medical Council was set up by the government of the day, not in the interests of the medical profession as is sometimes thought, but to safeguard the public by publishing a register of legally qualified doctors and by demanding a certain specified minimum of medical education. The Council supervised the examinations of the numerous licensing bodies in the country, in addition to those of the universities and medical schools.

The name of a doctor can be struck off the register by the Council for unprofessional conduct, and from this sentence there was until quite recently no appeal. However, a name once erased can be restored by the decision of the Council if the offender is judged to be once again worthy. Association with unqualified persons, canvassing for patients, and employing unqualified assistants are all considered unprofessional conduct, as well as the offenses that more commonly appear on the front pages of sensational newspapers, such as adultery with a patient and driving an automobile while under the influence of alcohol or drugs. In the eyes of the public, this registration is the chief function of the Council, but in fact its more important functions are improving medical education and supervising an official pharmacopeia of recognized new drugs and their methods of preparation.

The General Medical Council for Great Britain and both parts of Ireland now consists of 47 members: eight nominated by the Crown (three nonmedical, one of them a woman); 28 chosen by the universities, teaching schools and licensing authorities, such as the Society of Apothecaries and the Royal Colleges of Physicians and of Surgeons in England, Scotland and Ireland; and 11 members, including one woman, elected by the registered medical practitioners in the different parts of the country.

Postoperative psychoses—At a meeting of the Royal Society of Medicine, Dr. B. B. Zeitlyn of Cambridge presented a study of this subject undertaken jointly with Professor Stengel and Mr. E. Rayner. The term "postoperative psychoses" refers to mental illnesses which follow surgical operations. These conditions have received but little attention from psychiatrists, and the psychiatric textbooks either do not mention them or usually consider them with the delirious or toxic-exhaustive states.

Fifty-eight women patients and 22 men patients were studied, and despite the wide range of operations encountered the predominance of women and the high proportion of gynecologic operations were noteworthy. In no case could it be said that the anesthetic precipitated the psychosis. (That is, the signs and symptoms of the postanesthetic syndrome were not observed.) The type of reaction that was found was affective in 46 patients, schizophrenic in 12, confusional in 21, and neurotic in one. There was no evidence to suggest that abdominal or gynecologic operations are more likely than others to be

(Continued on page A-90)

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followed by psychoses, but hysterectomy appears to carry a greater risk than other gynecologic surgery. The age factor is a possible explanation.

In conclusion, it can be said that there is no evidence for the existence of postoperative psychosis. Its clinical status is similar to that of puerperal psychosis, which likewise manifests itself in a variety of common reaction types. It is of interest in this connection that some patients in the series had a history of both puerperal and postoperative psychoses. The development of psychosis in an individual depends on predisposing factors, with operation or childbirth as the precipitating cause. The role of emotional factors, assumed to be important for both, remains uncertain at least as far as postoperative psychoses are concerned. Would a psychosis have developed in these patients if they had not had their operations? They probably would not have had that psychosis at that particular time, but would have had it at some other occasion and precipitated by some other stressful event.

FRANCE

Hemoglobic cycle of iron in the organism—Using an electron microscope, Marcel Bessis conducted studies on ferritin and the hemoglobic cycle of iron in the organism (*Bulletin de l'Académie nationale de médecine*). The ferritin molecule, which was clearly visible under the microscope, has a diameter of approximately 30 Å., is composed of about 2000 atoms, and contains 23 per cent iron in four visible piles. Bessis traced the course of these molecules from the moment of their formation in the organs.

The red blood cells perished in the liver, spleen and bone marrow in 5 to 15 minutes; the vacuoles appeared first in the erythrocytes and then underwent hemolysis. Numerous scattered molecules of ferritin were formed around the fragments of red blood cells, and it appeared that these molecules could be formed independently of the red cells at the expense of iron stored in the viscera. Small groups of ferritin molecules agglomerated in large piles, which were visible under an optic microscope; these are the classic depots of hemosiderin.

The red cell-producing (erythroblastic) islets of bone marrow contained reticulum cells packed with ferritin molecules. The ferritin molecules left the reticulum cells and coupled themselves with the membranes of the erythroblasts, penetrating the latter by invagination as if they were aspirated by the cells. The edges of the invagination were then pinched off; a vacuole was formed, of which the wall ultimately disappeared, and the liquid content was later absorbed. The ferritin molecules were thus enclosed in the erythroblast. This type of invagination has been termed "ropheocytosis" by Policard and Bessis; it differs from pinocytosis, the usual course of invagination of fluid droplets.

At the time of the transformation of erythroblasts into red blood cells, the ferritin piles were absorbed and hemoglobin appeared. The final residue of ferritin was represented by the mitochondria, which ultimately disintegrated and disappeared in the mature red blood cell.

In various types of anemia, particularly Cooley's anemia, and in lead poisoning, the ferritin globules remained in the mitochondria and assumed the shape of dust. These iron-containing micelles were freed in the cytoplasm by the breaking up of the mitochondria, but they were not absorbed. The iron remained surplus and did not become part of the hemoglobin. This type of anemia differs from hemochromatosis, in which the red blood cells do not carry excess ferritin.

Mushroom poisoning—In a biologic study published in *La Presse médicale*, Leon Binet and Michele Leblanc asserted that poisoning from *Amanita phalloides* is the most common type of fatal mushroom poisoning in France.

In earlier studies, Binet proved that the low level of blood sugar is a direct cause of death in this type of poisoning. Tissue glycogen almost completely disappears, and hepatic glycogen entirely vanishes. The concentration of glutathione in the muscles and liver is markedly reduced. Blood coagulation is decreased. Recent investigation has shown a significant increase in the amount of fats, of free and ester-bound cholesterol, and of the unsaponifiable substances; this increase involves first the organs, particularly the liver, and subsequently the blood plasma and muscles. In the hours before death, the lipid level increases 5 to 15 times, according to the specific substances. The accumulation of lipids accompanies steatosis of the liver and the lowered level of blood glucose.

After conducting experiments with rabbits,

(Continued on page A-92)

growing clinical testimony

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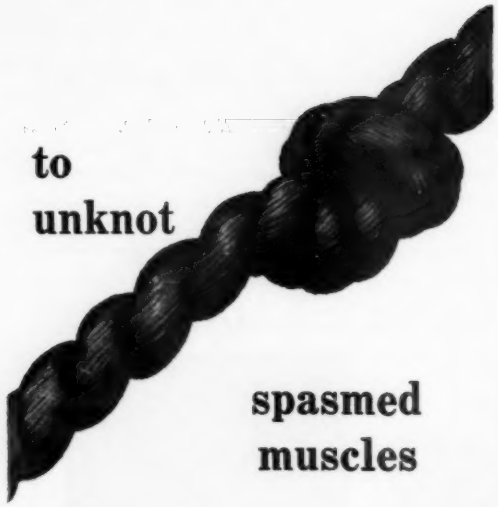

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SPAIN

Heart-lung pump—In the first use of the heart-lung pump in Spain, Dr. Gregorio de Rabago Pardo performed a pulmonary artery dilatation at the Clínica de la Conception, a branch of the Clinical and Medical Research Institute in Madrid. Previous work with the heart-lung unit had been confined to experiments with dogs.

The heart-lung machine used on the first human patient was presented to the Institute by Jaime del Amo. It changes the oxygen in the blood by means of an aspirator-impeller oxygenator. After extracorporeal circulation is established, the aorta is blocked off, and acetylcholine is injected into the arteries to stop cardiac action. The heart can be opened, and an immobile, dry field is attained. Graphs indicating circulation, oxygen saturation of the blood, and blood pressure in various circulatory sectors help to regulate the surgeon's action. After the cardiac defect is corrected, independent heart action is restored.

The operation performed by Dr. de Rabago was successful. The patient was a young man who had a narrowed pulmonary artery.

Dr. de Rabago, who spent two years specializing in heart surgery at medical centers in the United States, stated that acquisition of the heart-lung machine will enable qualified Spanish physicians to perform operations that they were formerly unable to undertake.

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HAEMOPHILUS INFLUENZAE
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Through the Stethoscope

NOAH D. FABRICANT

Doctors and Science Fiction

For some time, science fiction has provided pleasure and enlightenment for the cultural and scientific leaders of the nation, many of them physicians. While there is no generally accepted definition of the term, perhaps this one will do: Science fiction is that branch of literature which is concerned with the impact of scientific advance on human beings. Actually, science fiction often deals with the world of the future, a world in which social, economic and political boundaries have been shaped by the expansion of scientific knowledge.

One of the fascinations of this branch of imaginative literature is the way in which many of its authors have presented fanciful extrapolations of contemporary medical science. Their stories cover the entire spectrum of medicine, from allergy to surgery, from obstetrics to psychotherapy, from epidemiology to genetics. Sometimes medicine is the major element in the stories; frequently, it is part of the science fictional background in tales about other matters. In medical science fiction, the sky is not the limit at all; the universe can barely contain it. A few of the better stories are described herewith, to tempt more physicians into discovering the delights of this most modern of all forms of fiction.

It required the imagination and intellect of H. G. Wells to remove stories about interplanetary travel from the superficial adventure realm and to emphasize its future implications. In one of his stories about a trip to the moon, he emphasized the psychologic tensions and strains prevalent among the participants of the flight. Many interplanetary stories deal with Earth man's conflict with the people or things inhabiting other planets. One author points out that spaceships might require routine epidemiologic control of exotic diseases. Samples of air would be taken on landing and studied for identification of the organisms. After that the ship would be "sterilized" and the danger considered over. That such complications are most likely to ensue is seriously being considered by physicians, epidemiologists, psychiatrists and engineers currently engaged in planning extraterrestrial travel within the next decade or so.

In 1932, Aldous Huxley wrote about the dangers of Utopia in "Brave New World." He not only discussed "feelies," "orgy-porgy" and centrifugal "bumblepuppy" (as yet unrealized), but also wrote about an elaborate system of artificial reproduction and prenatal conditioning. Huxley accurately forecast the tranquilizer drug era of today. In "Brave New World," almost everybody was convinced that he was happy, for the drug taken was "euphoric, narcotic, pleasantly hallucinant . . . a gram is better than a damn." More recently, Wyman Guin foretold the universal use of a hypothalamus-blocking agent at the end of the twentieth century which "ended the great paranoid wars and saved mankind." Its action

(Continued on page A-108)

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1. Traylor, J. B., and Turpin, R.: Am. J. Obst. & Gynec. 61:71-74 (Jan.) 1951.

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Perhaps the most common branch of medical science fiction deals with matters that might actually happen today. Among the most brilliant of all medical science fiction is Lester Del Rey's "Nerves," which describes the horrifying results of an accident in an atomic power plant. At the opposite pole, Theodore Sturgeon, in "Twink," describes the feelings of a man who is a "sensitive," and who is able to communicate with his daughter *before* she is born. Obstetricians will be interested in Sturgeon's fictional handling of a cesarean operation.

Aliens from outer space have provided many imaginative medical situations. In "Bedside Manner," William Morrison writes of a man and woman, almost killed in a space accident, who are rescued and miraculously "rebuilt" so different from their human counterparts that they will not even let themselves be seen. The story involves cosmetic surgery on a truly vast scale. In a different vein, there is Eric Frank Russell's "Impulse," which describes how an English physician disposes of an invasion of malignant microscopic entities from space which take over his patient's dying body and temporarily bring it back to hideous life. This story has been compared with Poe's "Facts in the Case of M. Valdemar."

Medicine in the future is treated in a story by the late C. M. Kornbluth, in which superimproved antibiotics and electronic machinery reduce the art of diagnosis to childlike simplicity. Doctors merely attach a diagnostic gadget to the patient, then read a cure directly. Surgeons, on the other hand, use instruments that instantly heal wounds through stimulation of new tissue growth.

In still another story, Kornbluth tells about the horrendous results of permitting use of tomorrow's medical technical advances in a criminal society of our own era. And for neurosurgeons, Alfred Bestor provides this operative technic in a recent story: "Every nerve plexus had been rewired, microscopic transistors and transformers had been buried in muscle and bone, a minute platinum outlet showed at the base of his [the patient's] spine. To this [was] attached a power pack the size of a pea." In yet another surgical category, grafted prostheses replace lost arms and legs, and organ banks supply replacements for diseased structures. A story by Edson McCann pictures a method of growing new tissue *in situ* without grafting.

For physicians everywhere, science fiction contains some clues to modern thought about medicine. It is conceivable that the future expectations of medical science, as foretold in many medical science fiction stories, will eventually come true. Who can say that it is impossible to eliminate neuroses, conquer aging and cancer, provide spare parts for the human body, eliminate cardiovascular diseases, or postpone death for longer and longer periods? In the hope of encouraging physicians to turn to science fiction as a reading hobby, the writer of this column modestly announces that he is completing the gathering of material for a book of stories dealing with medicine in science fiction and fantasy. His collaborator is the well-known science fiction anthologist and authority, Groff Conklin.

The Higher Education

(Portrayed by Richard Gordon in "Doctor in the House")

One of the tests for prospective obstetricians was provided by a life-size papier-mâché model of half the female trunk, into which a straw-stuffed baby was slipped through a trap door. The candidate was then provided with a pair of obstetric forceps and required to deliver it *per viam naturalem*. This was demanded of Benskin. He solemnly applied the two blades to the head, taking care to put the correct one on first. He locked the handle, took it in the approved grip, and gave a strong pull. Nothing happened. He pulled harder, but the straw fetus refused to be born. He felt sweat on his brow and his mouth went dry; he saw his chances of passing fading like a spent match. He gave a desperate heave. His feet slipped on the polished floor and over his head flew mother, baby, forceps, and all.

The examiner looked at him lying on the floor for a second in silence. Then he picked up one blade of the forceps and handed it to Benskin.

"Now hit the father with that," he said sourly, "and you'll have killed the whole bloody family."

Research is proving that the abnormal manifestations of senility can be controlled, ameliorated and reversed. Success depends on the physician's understanding of and ability to control the abnormal behavior of elderly patients. While treatment with chemotherapeutic agents is often effective, special consideration should also be directed to nutritional problems. Total improvement, says the author, will be almost directly proportionate to the help and tender loving care the patient receives.

Our Senior Citizens — A Challenge With Hope

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THE good that medicine is doing is epochal; the sadness it is causing is clouding this victory over death.

The geriatric services of most of our hospitals, with their confused, bewildered and disoriented inmates hopelessly wandering to and fro or dejectedly sitting in well-worn chairs, exemplify this statement and present modern medicine with its bitterest challenge. Many of us have been indoctrinated with the idea that the elderly patients of these wards are untreatable. We were led to believe that they have entered a phase of organic deterioration which by its very nature is irreversible. Or we were told they have behavioral abnormalities which are the manifestations of arteriosclerosis or other malfunctions of the deteriorating organism. There is no help. There is no hope. These elderly patients are thought of as beyond the point of no return.

Challenging? It is more than challenging. It is heartbreaking, especially to those of us who have the foresight to see ourselves in such a situation—to see ourselves as addlepated residents of the present geriatric services of most of our hospitals.

We all know that medical science, education in public health matters, and higher standards of living have combined to extend the chronologic span of life in our society. Modern research has shown us that the usefulness of our senior citizens also has been extended—because there is no reason based on physical findings that says an individual cannot be efficient, productive and creative after he has reached the age of 65.

Knowing this, can we as doctors sit by and agree with those who say it is unfortunate that these forces did not also prepare the aged person to enjoy this longer life? We can, if we are unable to face the challenge our ever-increasing geriatric population puts before us.

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Assuming we are willing to accept the challenge, how do you approach it?

The man with a civilized mind is neither afraid nor ashamed to change it. Therefore you start by doubting, doubting that these elderly patients are untreatable, that they are beyond the point of no return. At Traverse City State Hospital we started this way and followed it by asking ourselves a simple question, "How can we help this forlorn segment of humanity to regain their rightful status as human beings?"

Four years of effort directed toward answering that question have been most revealing. We have not found a cure for aging, but the knowledge gained from our work with elderly patients has shown us that many of the manifestations of senility can be controlled, ameliorated and reversed.

As the full significance of what I have just said, that *research is proving that the abnormal manifestations of senility are treatable*, begins to register with each of you, you will begin really to think about it. You may start by thinking how this will affect one case or one problem close to you, but you will not stop there. With each new idea that your mind conjures up for you to explore you will come face to face with the realization that to receive the full benefits from these new findings you must readjust and re-evaluate many of your present concepts and your present approaches to the problems associated with the geriatric patient.

That, then, is the major impact research is having on geriatrics. *Research is forcing all of us to revise our thinking.* It is forcing us not only to tear down, brick by brick, our prejudices, our preconceived opinions and our former concepts about diagnosis, treatment and prevention, but also to adopt a new, straightforward, frontal attack on all aspects of the problems associated with elderly patients.

Doing this will not be easy and it will not always be successful, but it can be done. It is difficult to find ready acceptance of new ideas in a routine that has moved smoothly for generations. It will not always be successful because in terms of rehabilitation and treatment we find you cannot approach the problem of restoring the individual through one factor alone; you must deal with several, particularly the physical, the psychologic and the social.

To many of you this multivariable approach to treatment of elderly patients may sound complicated; and it is complicated to those of us who are doing research. However, if you dispense with the gobbledygook, the whereases and the whyfors and eliminate the complicated, complex and cumbersome research procedures you will find much that is applicable to the geriatric problems you meet daily. How do we know this? Because elderly patients do not arrive at our hospital with fancy psychiatric diagnoses any more than they arrive that way at the family physician's office. They all come to you and to us for exactly the same reason—either they cannot live with themselves or they cannot live with others in their communities. But you say this is too vague. What is it, specifically, that brings them to the general practitioner—and then to us at the state hospital?

The simple answer comes out of a study of many complaints leading to admission. It boils down to behavior, behavior of such an abnormal caliber that those closest and dearest to the oldster could not endure it any longer. All of you are familiar with abnormal behavior of this type. It existed thousands of years before its description in the learned nomenclature of Bleuler and Sigmund Freud. Yet because the mental abnormalities of elderly persons have been identified, tagged and labeled, and because all of us have become familiar with these terms, we are prone to see the end result, the mental changes. We see the evidence of confusion, disorientation and loss of memory, yet often fail to realize that it is not the mental changes but the abnormal behavior of the individual that has brought him to our attention. In fact, your ability to control the abnormal behavioral manifestations of the elderly patient is frequently the difference between successful care at home and commitment.

Therefore, before you start your treatment of elderly patients, before you see a single patient, it is necessary that you disregard the psychiatric diagnostic aspects of the problem. Do not misunderstand me; emotional and psychiatric problems are present. Most of the

emotional problems you will encounter are a result of social and economic phenomena. Many of the psychiatric problems of senescence are related to conflicts and experiences of earlier life and to lifelong unhealthy patterns of reaction. They are also related to altered status in the family and the community and to the inevitable signs of physical decline.[1] However, because no other psychiatric situation responds better to suggestion, interest and symptomatic treatment, a direct approach in this area is not needed if you will incorporate the art of medicine in your therapeutic regimen.

The art of medicine, as we use it, denotes an understanding of the emotional pressures peculiar to the old people of your practice, the possibilities of modifying their way of life, their attitudes toward themselves, and the emotional climate that surrounds them. It also means that you approach the elderly patient as treatable—and in a manner you would expect were your positions reversed.

Obviously, then, when treating elderly patients the first thing you should do is show them you are interested, that you care. Superficially this requires little more than a smile and a friendly greeting. However, to the elderly patient it has great therapeutic value. It conveys to him the fact that he has an understanding physician who will see him, respect him and listen to him. It makes him feel he is a participant in life—one of his greatest needs.

The time needed to establish rapport and the success or failure of your treatment may depend on the patient's reaction to this first meeting. Some elderly patients, because they are confused and disoriented, may give you the impression you are not getting through to them. Don't let this fool you. Approach every elderly patient, regardless of their abnormal behavior, as if they are understanding every word you are saying. This is quite important. These same confused, disoriented patients, after you have helped them and relieved some of their difficulties, often will tell you that were it not for your belief in them at the start they would not have been able to follow your instructions. They and their relatives are always most grateful.

Treatment of Abnormal Behavior in Elderly Patients

Having accepted the challenge presented by our senior citizens, it is only natural to ask, What do we treat and how do we treat it? More specifically, you would like to have the details of a therapeutic regimen for your elderly patients that would assist in their management at home. This I will endeavor to describe.

The best therapeutic regimen for treatment of the abnormal behavioral manifestations of your elderly patients should consist of at least three basic parts, although in actual practice you cannot separate one part from the others as easily as you can in a discussion such as this. One part should include an understanding of the abnormal behavior and the best treatment of each patient—individually. Another part would incorporate a program for the patient as a whole—his physical well-being, yes, but most important, in terms of abnormal behavior, his nutrition. The third part of the regimen, although quite important, does not have a specific plan. It is the help you can give these patients to accept themselves and the modifications imposed by their changing circumstances. It would also include enlightenment of the relatives and the community.

Use of Drugs

What is abnormal behavior? How do we treat it? Our treatment of abnormal behavior is basically chemotherapeutic in that we start with the new neuropharmacologic agents. The program itself is simple, but before it can be successfully executed it is mandatory that you understand these new drugs—their limitations, their good and bad points, the results of their prolonged clinical use. This is important, because these new drugs have specific indications and contraindications. The same is true of abnormal behavior. You must understand its manifestations, its changes and its relationship to drugs.

The logical place to find these answers is the literature. During the past three years there have been more than 5000 scientific papers on the new drugs. If one were to read

and abstract all of these, it would lead to but one conclusion, that "the new-drug situation is a mess." This is true because in most cases these drugs are being used to treat diagnoses instead of patients. Most of the new drugs act primarily on abnormal behavior and secondarily on mental mechanisms. It makes a difference whether the behavior is associated with overactivity or underactivity, as most of the new drugs are specific for one type or the other. To understand their effects it is necessary to think of them primarily as drugs for treating behavior and, as I said before, to disregard the psychiatric diagnostic aspects of the problem.

Knowing that the new drugs are rather specific for one or the other type of behavior (overactive or underactive), it is evident that none of these drugs will control all behavior problems—regardless of reports in the literature. This simply means that today we do not have a single drug that will control all behavior problems, mainly because, as with most other balanced reactions of the body, behavior usually is a combination of overactivity and underactivity. This is true of normal as well as abnormal behavior. None of us carries a full head of steam all the time, just as none of us has his fires banked all the time. However, most of us are able to control ourselves and consequently can live with the stresses and strains that confront us each day. When the response of an individual to the pressures of life is such that he cannot control himself, then we have abnormal behavior. The abnormality may be well covered up, or it may be severe enough to disturb other people.

I cannot give you a 1,2,3 plan for diagnosing treatable behavior, but I can say that each of you is doing it every day. Take the patient who comes into your office with or without specific objective pathologic signs; before you have talked to her two minutes you have mentally recorded the fact that she is tense and nervous or has the blues or is down in the dumps. With few exceptions, however, behavior is mixed in character. That is, in most patients, regardless of the outward behavioral manifestation, there is an element of the opposite present. Let me repeat: In most patients, regardless of outward manifestations, there is an element of the opposite behavior present. We have stressed this mixture of behavior within each patient because an understanding of it will greatly increase your success with the new drugs and eliminate many of the difficulties you may be encountering.

A combination of drugs—one for overactivity and one for underactivity—is more effective than either drug when used separately. Which drugs should you use? The literature, loaded as it is with ambiguous and contradicting statements, makes a true study of each drug impossible. What, then, are you to do? Concentrate on one analeptic and one tranquilizer. Study them, know them, use them, and understand them clinically—separately and combined. For most of your behavior problems they will be enough.

During the past five years we have investigated 49 new drugs. Many of these are highly active and are useful in special cases. However, for simplicity of administration, minimal incidence of side reactions, and uniformity of good results we feel that two drugs, reserpine (SERPASIL®) and methylphenidate (RITALIN®), are adequate for everyday use in treating the abnormal behavioral manifestations of elderly patients. Serpasil is a tranquilizer and is therefore useful in treating overactive behavior. Ritalin is a psychoanaleptic, a mental awakener. It is useful in treating underactive behavior. Proper combinations of these two drugs will control, ameliorate or even reverse most elderly behavior problems. Age, length of illness, and the usual physical infirmities of elderly patients are not contraindications to the use of either drug.[2] Special diagnostic or laboratory technics are not needed, although we have used them in more than 800 cases. Clinical observations are the most important criteria for estimating both initial and maintenance dosages. If the medication is adjusted to the clinical picture the difficulties will be minimal and the benefits maximal.

The use of divided daily dosages will provide smoother action. We prefer a schedule of three doses daily—before, after or with meals. The tablets may be crushed and put in food or beverage if necessary.

Elderly patients showing a predominance of overactivity should be given Serpasil initially. A good starting dose is 0.2 mg. three times daily. Those showing a predominance of underactivity should be given Ritalin initially, starting with 10 mg. three times daily. Elderly patients who manifest mixed behavior, or about whom you are not sure, may receive both Serpasil and Ritalin initially. A good starting combination is 0.2 mg. of Serpasil and 10 mg. of Ritalin three times daily. With a wide margin of safety, these starting doses may be increased if necessary.

The first change may be observed within two or three days, or it may take as long as three weeks. Checking the patient every day or two during this period will allow for proper regulation of the dosage in order to produce the desired results.

As the clinical behavior pattern of each patient starts to shift toward normal, either the initial dosage should be reduced or the second drug should be added. In the case of an overactive elderly patient the objective usually is a reduction in motor activity, aggressiveness or anxiety and tension. When this decrease is observed clinically without any evidence of reduced mental activity, it is best to reduce the dosage of Serpasil gradually before adding Ritalin. If, on the other hand, the reduction in motor activity includes decreased mental activity, it is best to add Ritalin directly. In a few elderly patients, lethargy may be noted before the motor activity or aggressiveness is reduced. This condition is rare, but when it occurs a small amount of both drugs should be added—Ritalin to overcome the lethargy and Serpasil to take care of the motor activity.

Maintenance dosage for most overactive elderly patients is about 0.25 mg. of Serpasil and 5 mg. of Ritalin three times daily. About a fourth of these patients will require a larger regular dose of Serpasil.

In the senile group the number of underactive patients is about half or a third that of the overactive patients. A withdrawn, quiet patient loaded with tension, anxiety or resistance should be considered overactive and treated as such. Thus, a patient with a furrowed brow and sweaty hands who refuses to follow normal routines should be given Serpasil initially and treated as an overactive patient—even though he may try to put up a negative front. It is usually because of their confusion and disorientation that these patients resist. They do not understand, so they resort to survival tactics—fighting and resisting. A truly underactive patient is one without tension, anxiety or resistance. He can be confused or disoriented. Usually he requires help or prodding to follow daily routines. He follows easily, making few if any decisions for himself. Ritalin may produce clinical changes in such patients within a couple of days. If there is no change within three or four days the dose should be increased. If, after gradually raising the dose to 30 mg. three times daily, there is no change within three or four days, it is then advisable to add Serpasil. In most cases this will produce a change, and then the drugs can be balanced.

When there is improvement in the negative clinical pattern without evidence of excess motor activity or aggressiveness, the dosage of Ritalin can be reduced gradually. When there is clinical evidence of overactive behavior along with mental awakening, Serpasil should be added to the Ritalin. Most underactive patients will be maintained on about 0.2 mg. of Serpasil and 10 mg. of Ritalin three times daily.

The cause of abnormal behavior is not always known. There will be times when a balanced patient will be temporarily upset or depressed. Addition of extra amounts of Serpasil or Ritalin for a short time usually will help him through these periods. A comparison with the control of diabetes is in order. If the diabetic patient overeats, he takes more insulin. If he fasts, he cuts his insulin. A similar adjustment in relation to the amount of mental strain is needed in the treatment of elderly patients with behavior problems. The diabetic patient cannot make these adjustments unless the reason is explained to him, and therefore for best results in behavior problems it is necessary to explain to the patient or his relatives the action of each drug, the results expected from it, and the symptoms which should be reported to you so that you

may adjust the dosage properly in order to reach the desired goal, active tranquility.

After the patient has reached a balanced state the dosage of both drugs can be reduced gradually to the maintenance level. In some cases the drugs can be eliminated, but senile patients usually do better and have a smoother life if kept on a maintenance dosage. Moreover the relatives demonstrate less anxiety if the medicines are continued.

Not all senile behavior is grossly abnormal when first it comes to the attention of the family doctor. Consequently there is a large group of elderly patients who need some mild medication for anxiety and tension states—a mild tranquilizer without the sedative or habit-forming properties of the barbiturates. For these patients we have found that NOSTYN® (2-ethyl-*cis*-crotonylurea) induces the best clinical response. In a dosage range of 150 to 300 mg. three times daily, its mild action promotes an over-all calmness that makes the patient easier to manage and more capable of participating in activities. The low dose required for sedation and the comparatively high dose required for hypnosis make it a valuable drug for senile patients who do not tolerate the more potent tranquilizers.

The "Extra Touch"

While it is possible with three drugs—Serpasil, Ritalin and Nostyn—to control, ameliorate and prevent the abnormal behavioral manifestations of elderly patients, these drugs by themselves are not the answer. They do not have the power to restore the senile patient, although they can produce within him the ability to participate. Total improvement will be almost directly proportionate to the amount of help and tender loving care that the patient receives.

"Help" and "tender loving care" carry a special connotation. To us, they are symbolic of the extra touch, the special considerations you can give your patients that will allow them to participate in a richer life. Both should be part of all therapeutic regimens for management of elderly persons. Sometimes this extra touch, this special consideration may be a taken-for-granted thing. A cane, a reading glass, a rocking chair or a better be[illegible]-each of these, if needed, would bring hou[illegible] of enjoyment to an oldster.

Physically this extra touch may [illegible] good foot care and proper shoes. Corns, [illegible]lluses and poorly fitted shoes cause the best [illegible]f us to limit our activities, and may keep you[illegible]lderly patient in bed if not corrected. Glasse[illegible] and a hearing aid, if needed, will remove the cobwebs from your patient's vision and bring new music to his ears. They will also bring him into a better relationship with his environment.

Nutrition

Because there is a direct relationship between optimal nutrition and mental acuity, the most important of all these special considerations is the help you give your patient with his nutrition and his nutritional problems. If he is a poor eater, ill-fitting dentures and sore gums or any of a number of correctable oral or dental difficulties may be responsible. Poor eating may also be due to unattractive, unappetizing meals. On the other hand your elderly patient may eat too much. This, too, should be corrected.

The eating habits of elderly patients, their choice of foods and the amount ingested, usually are the result of many years of conditioning and therefore difficult to change. In fact, if any of your elderly patients are not interested in or are not eating a diet that gives them optimal nutrition it will be easier to supplement it with in-between nourishment than to try to force a change of eating habits. For supplemental nourishment we find powdered milk preparations the most useful. They are easy to prepare, can be adjusted to nutritional needs, and with a little creative imagination offer sufficient variety to insure their continued acceptance.

Because so little is known about many of the metabolic processes of elderly persons, we have, as part of our geriatric research, been investigating the value of added vitamin-mineral preparations. The decreased morbidity and the improved physical and mental status of patients receiving this special supplementation have been so outstanding that we feel all elderly patients should include vitamins and

minerals in their nutritional regimen, not as a cure for aging but as metabolic supplementation—or, as Dr. Tom Spies[3] so ably described it, "for the relief of the minor aches and pains of older persons." However, vitamin-mineral preparations are not all the same, and the most highly advertised or the most expensive are not necessarily the best. Before you prescribe vitamins, read the label; then prescribe the best preparation obtainable for the needs of your patient.

When a therapeutic vitamin-mineral preparation is needed, we have found that VI-SYNERAL®, VITERRA® Therapeutic and CLUSIVOL® or Clusivol Geriatric give good results. When our patients have a poor appetite, are not interested in food, or are finicky eaters, we find the use of WHEATAMIN® Extract is most helpful. If the patient's nutritional problem includes anemia, the use of BEMOTINIC® with its wide range of antianemic components will be most helpful. These are but a few of the many good preparations we have used, but they serve to show the versatility of vitamins and minerals as aids in the management of the nutritional problems of elderly patients.

Because there is much that remains unknown concerning the relation of enzyme systems, metabolic processes and vitamins to the physical and mental well-being of elderly persons, a major portion of our present research is devoted to investigation of separate vitamins and special combinations of vitamins and minerals. One of these new preparations is known as MRD-450. It contains 100 mg. of niacin and 20 mg. of FRENQUEL® per teaspoonful. Given in a dosage of 1 teaspoonful three times daily to elderly patients who present clinical evidence of confusion, we find that it clears this confusion measurably. MRD-450 is not on the market, and the niacin in it may produce a flush reaction. Nevertheless because of its favorable action in relation to mental acuity we feel it will be well worth your time to secure a supply for clinical trial.

Other compounds we are investigating show promise of controlling tremors, reducing capillary fragility, increasing anabolic activity and, in general, improving the physical and mental status of elderly patients. Each day brings new results that give promise of new understanding and better treatment for them. How long it will take to find all the answers I do not know. I do know that by your early detection and conscientious treatment of the abnormal behavioral manifestations of your patients you will make this a much better world in which to grow old.

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Twenty cases of resection of the abdominal aorta with insertion of homografts are reviewed. In 19 of these cases the aneurysms were arteriosclerotic. The most difficult part of the operation was in separating the inferior vena cava from the aneurysm; the most common complication was thromboses. In view of the survival period and relief of symptoms obtained in this series, the authors believe that this comparatively new operative procedure is logical and worthwhile.

Results of Treatment of Aneurysm of the Abdominal Aorta

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RESECTION of aneurysms of the abdominal aorta with the insertion of homografts has proved logical and worthwhile. This operation was devised because of the high mortality rate associated with untreated aneurysms[1-3] and because of the unsatisfactory results of the treatment used previously.[2,4,5] Although this operation first was performed more than five years ago,[6,7] it has been performed in a significant number of cases only in the past two or three years. For the proper evaluation of a new operation, it is necessary to analyze the results frequently, even if a large number of patients have not been followed for a long time after the operation. Mortality, morbidity and the results of the operation must be compared with those in cases in which other types of treatment have been used and with the natural history of the untreated disease.

With these thoughts in mind, we have made a study of 20 cases of aneurysm of the abdominal aorta in which this operation was performed at the Lahey Clinic over a year ago.

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Clinical Data

Sixteen of the 20 patients were men and four were women. The ages of the patients ranged from 45 to 79 years, and the average age was 59 years. Most of the patients had symptoms attributable to the aneurysm, but

TABLE 1

PREOPERATIVE SYMPTOMS AND RESULTS OF OPERATION

PREOPERATIVE SYMPTOMS	CASES	DURATION OF SYMPTOMS	RESULTS		
			Dead	*Symptoms still present*	*No symptoms*
None	3		0	1	2
Abdominal pulsation	4	9 mo.	0	1	3*
Significant pain	13	23.8 mo.	5†	2	6
TOTAL	20		5	4	11

*One patient, who was free of symptoms when dismissed, was known to be alive seven months after the operation, but no other information was obtained.

†Two of these patients died before they were dismissed from the hospital.

three did not have any symptoms (table 1). Abdominal pain was the most frequent symptom, but exertional claudication and back pain occurred in almost a fourth of the cases. In two cases, nausea and vomiting were present when the patients were admitted to the hospital, and one patient was in shock due to rupture of the aneurysm.

The blood pressure was normal in 11 cases, and it was markedly elevated in only one case. In this case, it was 220 mm. systolic and 120 mm. diastolic. The aneurysm was palpable in 16 cases and pulsatile in 14 cases. The results of examination of the abdomen were completely normal in only three cases. Pulsation in the lower extremities was normal in 12 cases and diminished in five cases. It was not recorded in three cases.

Laboratory Findings

Of the laboratory examinations, roentgenography was most helpful. At first, aortograms were made regularly, but as our experience increased they were made only in cases in which there was some doubt about the diagnosis or resectability of the lesion after physical and roentgenographic examination of the abdomen had been performed. Most aneurysms of the abdominal aorta do not extend above the renal arteries, and exploratory laparotomy always is necessary to determine whether or not the aneurysm is resectable. We have not decided that operation was contraindicated on the basis of the aortographic findings. The percentage of error has been about the same with the aortogram as it has been with the plain roentgenogram. In 17 of 19 cases in which plain roentgenograms were made, the roentgenographic appearance was diagnostic. The roentgenograms showed evidence of calcification in 15 cases. In one of the two cases in which the aneurysm was not visible on the plain roentgenogram, the diagnosis was made by aortography; in the other case, the diagnosis was not made by this means. In this case, the preoperative diagnosis was thrombotic occlusion of the aorta.

In 13 of the 15 cases in which aortography was used, the aortograms were diagnostic. In the two remaining cases, the aortograms were abnormal. In one of these cases, the aortogram disclosed narrowing of the aorta; in the other case, it revealed irregularity of the aorta. In the latter case, the diagnosis was made by means of the plain roentgenogram. Atelectasis of the lower lobe of the left lung was the only complication observed after aortography.

None of the roentgenograms disclosed evidence of vertebral erosion, although operation revealed definite vertebral erosion in one case and questionable erosion in another case.

Serologic tests for syphilis were performed in 14 cases, and the results of the tests were negative in all of these cases. An electrocardiogram was made in 16 cases, and it was normal in 11 of the 16 cases.

Pathology

In 19 of the 20 cases, gross and microscopic examination revealed that the aneurysms were arteriosclerotic. In the remaining case, the examination disclosed only medial degeneration of the aorta. An intraluminal thrombus was present in almost all of the cases, and the lumen was obliterated in some cases. The largest aneurysm was 10 cm. long and 11 cm. in diameter. The aneurysm extended into and involved one common iliac artery in three cases and both of the common iliac arteries in four cases.

In four cases, an aneurysm was present in vessels other than the abdominal aorta. An aneurysm also was present in the aortic arch in two cases and in the common iliac artery in one case. In the remaining case, an aneurysm was present in the right common iliac artery, in the left subclavian artery, and in the coronary artery, in addition to the one in the abdominal aorta.

As might be expected in cases in which the patients are between 45 and 79 years of age, associated or coincident disease was present in several of the cases. Arteriosclerosis of other vessels was present in several of the cases, and in these cases calcification was revealed by roentgenographic examination or by palpation of the vessels at the time of operation.

There was a history of myocardial infarction in one case, and of diabetes in two cases. Two patients had had angina pectoris. One of the patients had cerebral arteriosclerosis. Peptic ulcer was or had been present in four cases. There was a history of cholelithiasis in two cases, of arthritis in one case, and of diverticulosis in one case. At the time of the primary operation for the aneurysm, cholecystectomy was performed in the two cases in which cholelithiasis was present.

Operation

It was possible to insert a segmental graft in only 4 of the 20 cases. In one of the 16 cases in which a bifurcation graft was used, the internal iliac artery was ligated and divided, and then was anastomosed to the external iliac artery. In another case, an anastomosis was made with the external and internal iliac arteries on one side. The aorta was clamped for periods ranging from 30 to 170 minutes. The average time that the aorta was clamped was 85 minutes. Bilateral lumbar sympathectomy was performed in 19 cases.

As a rule, the most difficult part of the operation is separating the inferior vena cava from the aneurysm. In two cases, it was necessary to ligate the vena cava. In one of these cases, the patient died, but there was no evidence that the ligation of the vena cava had contributed to the patient's death. In the other case, the patient has been free of symptoms for one year and two months after the operation, and there has not been any evidence of edema or circulatory impairment, either venous or arterial, in the lower extremity.

Complications

An operation of the nature and magnitude of the one we are describing inevitably will be followed by complications, both those peculiar to the operation itself and those associated with any major abdominal operation. A total of 22 complications occurred in 14 cases (table 2). Six patients had no complications.

TABLE 2

POSTOPERATIVE COMPLICATIONS IN 14 CASES

COMPLICATIONS	NUMBER
Thrombotic	
Arterial	5
Venous	3
Pulmonary atelectasis	2
Infection	
Abscess of buttock	1
Cystitis	1
Miscellaneous	
Jaundice	
Immediate and transient	1
Two months after operation	1
Disorientation from narcotic	1
Wound hematoma (femoral arteriotomy)	1
Pancreatitis	1
Anuria	1
Obstruction of ureter	1
Hiccups	1
Ileus	1
Painful leg	1
TOTAL	22

Eight of the complications were thrombotic (five arterial and three venous). Amputation of the thigh was necessary in one case, and it would have been performed in two other cases if the patients had lived. In two cases, amputation was averted by a second operation. Some of these thrombotic complications occurred early in our experience with this operation and before we were sufficiently aware of the possibility of the complication. In spite of all precautionary measures, however, this complication occasionally will occur after the operation. Although we carefully watch for changes in the pulsation, color and temperature of the lower extremity, pain and loss of function in the extremity are the findings most suggestive of arterial occlusion.

In order to prevent this complication, we now inject heparin into the iliac arteries immediately after they are clamped. After the anastomosis with the aorta has been completed, one iliac artery is allowed to "backbleed" and if a clot is present it is aspirated. More heparin is injected, and the anastomosis is made. The same procedure is repeated before the second iliac anastomosis is made. We have not used general anticoagulant therapy except in three cases in which thrombophlebitis occurred.

Mortality

There were two deaths in the immediate postoperative period. One patient died of hypertensive cerebral disease 13 days after the operation. The blood pressure was 220/120. At the time of her death, the patient had early gangrene of her right foot as a result of occlusion of the anterior tibial artery. The other patient died of anuria, pancreatitis and gangrene of the left leg 11 days after the operation. The blood pressure was 170/100, and the patient had an aneurysm of the right common iliac artery, the left subclavian artery and the coronary artery.

There were three late deaths. One patient died of myocardial infarction and pulmonary edema eight months after the operation. Necropsy revealed that the vessel was patent at the site of the graft. The other two patients died of a late complication which has been seen by other surgeons but which has not been discussed frequently in the literature. One of these patients died two and a half months after the operation, and death was due to hemorrhage into the distal portion of the duodenum from the site of the upper anastomosis. This was the only patient in our series who had an aneurysm which involved a renal artery. The anastomosis in this case had been difficult technically.

The second patient had similar bleeding. An exploratory operation was performed elsewhere, but the source of the bleeding was not found. Because the bleeding continued, another operation was performed 10 days later, and a fistula between the aorta and the duodenum was closed. Bleeding recurred, and another operation was performed 10 days after the last one. At this time, a patch graft was placed over the fistula. Three weeks after this final operation, when the patient apparently had made a good recovery, he died of a myocardial infarction. We know of another case in which this complication has occurred. In this case, the operation was performed elsewhere. Wilson[8] has told us of still another case, and Brock[9] has given a description of a similar complication.

In order to prevent this complication, the anastomosis should be made with as much care as possible, the aneurysm should be resected so that there is minimal disparity between the size of the graft and that of the host's aorta, and, finally, the peritoneum should be closed so that it lies between the site of the anastomosis and the duodenum. Perhaps, as Cooley[10] has suggested, if grafts must lie in a large hematoma (that is, if the operation is done for a ruptured aneurysm), the omentum should be placed between the graft and the duodenum.

Results

Seventeen of the 18 patients who survived the operation have been followed for more than a year. All of these 17 patients have been seen by physicians, many of them by physicians at the Clinic, and others by referring physicians. The patient who was not seen by a physician was known to be alive seven months after the operation.

The result was excellent in 13 of the 15 cases in which the patients were known to be living when this paper was written. In all of the 13 cases, the patients were free of symptoms (table 1). In one of the two cases in which the result was unsatisfactory, the patient was free of symptoms immediately before the operation, but he now has slight claudication on exertion. The other case is the one in which the thigh was amputated because of a thrombotic complication.

Two patients are much improved although they still have mild claudication on exertion. One of these patients had had severe claudication before the operation, and the other one had had severe pain in the back.

These results may be compared with those in cases in which the aneurysm is not treated. Estes[3] reported 102 cases of aneurysm of the abdominal aorta in which the patients were not treated surgically. Of 91 patients who were traced for one year, 61 were still living. The survival rates in cases of asymptomatic aneurysm were similar to those in cases of symptomatic aneurysm.

De Takats and Marshall[2] found that seven patients with untreated aneurysm of the abdominal aorta died within three years after the diagnosis was made. Four of the seven patients died of the aneurysm. The average period of survival was about 18 months. The same authors made a follow-up study in 10 cases in which the patients were treated by one of the methods intended to produce fibrosis around the aneurysm. The average period of survival after the operation was 16 months and the longest period was four years. At the time of this study, seven of the patients were dead. Three of the patients died of the aneurysm, two died of myocardial infarction, and the cause of the death of the other two patients was not stated.

Cowley and Yeager[5] made a study of 15 cases in which the patients were treated in a similar manner. Seven of the 15 patients were dead when the study was made, and four of the seven died of the aneurysm. The average period of survival in the 15 cases was 15 months and the shortest period was two months.

Comment

Although the interval since the resection of the aneurysm and the insertion of homografts in the 20 cases has not been long enough to warrant definite conclusions regarding the value of this operation, the results, as judged by the period of survival and the relief of symptoms, appear to justify the use of this operative procedure. We believe that asymptomatic aneurysm should be resected if the condition of the patient will permit this operation.

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DISEASES OF THE SKIN—*First of a Series*

The Problem of Hand Eczema

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ECZEMA of the hands constitutes one of the most bewildering diagnostic problems for the physician, for the eruption may seem devoid of specific identifying features. A working classification of 10 major categories of eczema of the hands is proposed, since treatment without determination of etiologic factors may end in failure and since early detection of the cause of the condition may prevent lifelong disability.

Because of the multiplicity of factors in the etiology of eczema and because various types frequently overlap, the task of classifying eczema of the hands may at first seem complex. Yet if the primary lesion is scrutinized and the original pattern of the eruption determined, it will fall more easily into one of 10 major categories. The appearance and location of an eruption on the hands provide important diagnostic clues, and a meticulous history may be of infinite value.

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Classification of Eczema of the Hands

1. Contact eczema.
2. Infected eczema.
3. Mycotic eczema.
4. "Id" eruptions.
5. Nummular eczema.
6. Pompholyx.
7. Atopic dermatitis.
8. Food allergies.
9. Inhalant allergies.
10. Miscellaneous hand eczemas.

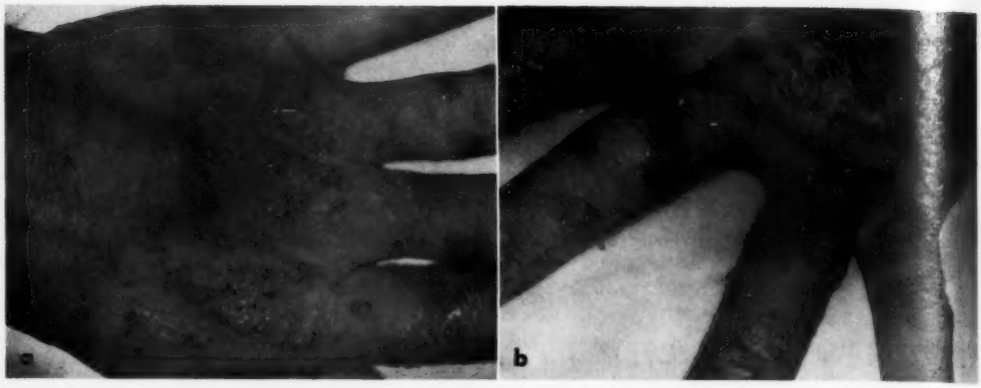

FIGURE 1a and b. Dermatitis venenata, eruption from fluids on dorsa of hands of an electroplater.

What Is Eczema?

Eczema is not a disease per se but a group of physical signs. It is the summation of a multitude of varying and variable insults to the skin, resulting in a composite of inflammatory reactions. Most eczemas begin with itching and some erythema. Vesicles and regular groups of small papules frequently follow. Secondary changes are extremely variable and may include weeping, fissuring, scaling, crusting, infection and often lichenification.

Disposition to Hand Eczema

It is enigmatic why hand eruptions develop in some persons and not in others exposed to the same environment. It would appear that the skin's ability to resist a variable onslaught of insults diminishes under certain conditions. Authorities have indicted numerous factors, e.g., allergic states, hyperhidrosis, anxiety, stress, malnutrition and debilitation.

FIGURE 2. Primary irritant dermatitis from fluids. Vesicular eruption on dorsa of hands.

1. Contact Eczema

Primary irritant dermatitis—Primary irritant dermatitis (dermatitis venenata) is an inflammatory reaction to definite known external irritants. If a person immerses his hands in a strong cresol solution a vesicular eruption will develop. Allergy or hypersensitivity need not be considered, since anyone's skin may react this way. Primary irritants (strong chemical or physical agents) are noxious to any normal skin, and this type of dermatitis is not characterized by acquired or specific features but is due to a cytotoxin acting directly on the epidermal cells. It is encountered frequently in industry. Causal agents include chemicals (formaldehydes, acids, alkalies, phenol), cleansers (distillates, strong soaps, turpentine), and physical agents (wool, glass, trauma, heat, plants, paints, cement). Dermatoses from fluids nearly always involve the dorsa of the hands, where the skin is thinner and more prone to trauma (figures 1 and 2).

Allergic contact eczema—Allergic contact eczema (eczematous sensitization) (figure 3) has been produced experimentally in man and animals. In this type there is an incubation

period. If a reaction occurs less than six days after initial exposure the person either does not have allergic sensitivity or has been exposed to the allergen previously. Development of allergic contact eczema does not necessarily mean exposure to a "new" substance. A person may become sensitized to something to which he has been exposed for years. A few examples of the many agents which produce contact eczema are stair railings, grapefruit, plastic hosiery, automobile gearshifts, purse straps, door knobs, knife handles, tennis rackets, and cedar wood in pencils. Dermatitis from an automobile ignition key may depend on sensitivity to nickel, and an eruption on a milker's hand may arise from sensitivity to cow's hair. "Wrist watch dermatitis" may involve the dorsum of the hand instead of the wrist if the watch has an extensible metal strap that is pulled over the hand. Each occupation or trade is prone to its peculiar pattern of hand eruption (plate 1). In the shoe industry the fitting of heels often causes a sensitivity to rubber. Carpenters may be sensitive to putty, and tailors to wool. Patch tests may help identify the causative agent if they are expertly made using only the exact recommended concentration of the agent.

The original pattern of the dermatitis should be studied, although at the patient's first visit it may be obscured by infection, secondary contact sensitivity or medication; or perspiration, pressure and friction may have intensified or modified it. The area of involvement often is the area of contact with the offending agent. Because of the wide variety of bizarre patterns, the cause of a contact dermatitis may be completely masked until a veritable Sherlock Holmes' medical history is obtained.

"Housewives' dermatitis"—Many authors have considered this common, poorly understood and often crippling eczema of the hands purely a contact dermatitis, others a psychosomatic disease, and still others a variant of nummular eczema. It has been said that when a woman has children she virtually becomes an amphibious creature. Constant exposure to hot water, soap and detergents, aggravation by fatigue and other stressful situations

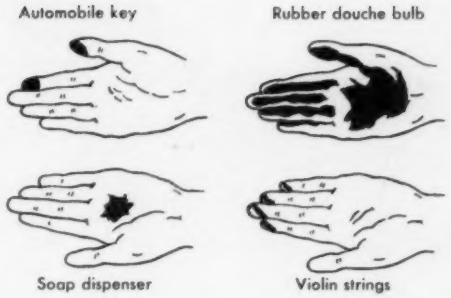

FIGURE 3. Various patterns of allergic contact eczema.

all contribute to the development of housewives' eczema. The wedding ring finger often is the initial site of the eruption, as the ring is a catchall for soap, sweat and debris.

Overtreatment of housewives' eczema unfortunately is all too common. These eruptions rarely are cured without complete avoidance of soap and water (including baths and showers), stopping all housework, and frequent bland soaks or compresses, followed by appropriate anti-inflammatory and anti-infectious topical treatment. The value of a vacation away from home and family is incalculable. For infected cases, systemic antibiotics may be required. On resumption of work the patient should wear clean white cotton gloves with the seam side out. If rubber gloves are worn they should be loosely fitted over thin white cotton gloves and never worn for more than 10 minutes at a time. Cotton-lined rubber gloves are not recommended, since the lining collects sweat, dirt, oil and dust, all chronic irritants.

Treatment of contact eczema is outlined in table 1.

2. Infected Eczema

Infected eczema is much more common than eczematized infection. In secondary infections, microorganisms do not play the leading role in initiating the condition but may be important in protracting and intensifying it. The lesions are quite variable morphologically and have a much less characteristic course than do primary infections.

Antibiotics have revolutionized therapy of

FIGURE 4. Infected eczema. Dermatitis venenata from fluids complicated by secondary bacterial invasion.

FIGURE 5. "Infectious eczematoid dermatitis." Infection and eczema both present in localized palmar distribution.

acute bacterial infections but have been disappointing in the more chronic eczematous skin infections. Before beginning therapy one should decide whether one is dealing with a primary pyogenic infection or a secondarily infected eczema of the hands (figures 4 and 5). A primary bacterial infection originates in previously healthy skin and usually has a characteristic morphologic appearance; examples are impetigo, folliculitis and furunculosis. When both eczema and infection are present, antibacterial therapy alone will not suffice. The eczema must be treated as well.

Although infection is very common, pathogenic organisms may proliferate to an astonishing degree in some skin lesions without causing significant injury. To determine the pathogenicity of organisms which have colonized diseased or eczematous skin, a simple smear made by swabbing the skin vigorously with a cotton tip may prove useful. A Gram stain is done and the slide is examined for leukocytes and bacteria. Bacterial phagocytosis by leukocytes is good evidence that a defense mechanism is in operation. Leukocytes do not necessarily indicate a specific reaction to bacteria, but their simultaneous occurrence increases the probability that they were called forth in response to infection. They usually will be absent on smears of lesions in which the pathogenic organisms are simple invaders. The fact that pathogenic staphylococci and streptococci are almost always present in moderately and severely infected eczema greatly reduces the value of culture and sensitivity studies.

Table 2 is an outline of the treatment of infected eczema.

TABLE 1

TREATMENT OF CONTACT ECZEMA

1. Search for and eliminate offending agents
2. Protective measures (white cotton gloves, barrier creams and ointments)
3. Avoidance of all irritant factors (soaps, detergents, chemicals, dust, hot water)
4. Rest
   - Local—Splinting of hand for fissured areas
   - General—Sedation and tranquilization as indicated
5. Perspiration control
   - Cool temperature
   - Anticholinergics (PAMINE®, 2.5 mg. t.i.d.; PROBANTHINE®, 15 mg. t.i.d.)
6. Topical measures
   - Acute—Cool soaks (Burow's solution, $KMNO_4$, boric acid, Dalibour's solution)
   - Emolliation—Cold cream, hydrophilic petrolatum, lanolin
   - Chronic—Mild tars, ICHTHYOL® 3 per cent in zinc oxide unguent
   - If infected—Antibiotic ointments (NEOSPORIN®, polymyxin)
   - Corticosteroid Rx—Topical hydrocortisone definitely aids regression of acute and chronic stages (use as adjunct to above measures)
7. Systemic cortisone or corticotropic therapy in severe advanced cases
8. X-ray therapy only in severe, refractory, persistent and crippling cases
9. Foreign protein therapy occasionally is of benefit as an adjunct in therapy

PLATE 1a and b. "Pattern-type" allergic eczematous dermatitis of first two fingers from plastic steering wheel. Patient was a taxicab driver.

PLATE 2. Primary moniliasis of fingers and nails (*C. albicans*).

PLATE 3a and b. Primary fungous infection of ankle (vesicular *T. rubrum* infection). Dermatophytid. Sterile vesicular secondary eruption on dorsa and sides of fingers.

PLATE 4. Nummular eczema. Coinlike lesions involving dorsa of hands.

PLATE 5. Pompholyx involving palms and sides of fingers. Hyperhidrosis is also present.

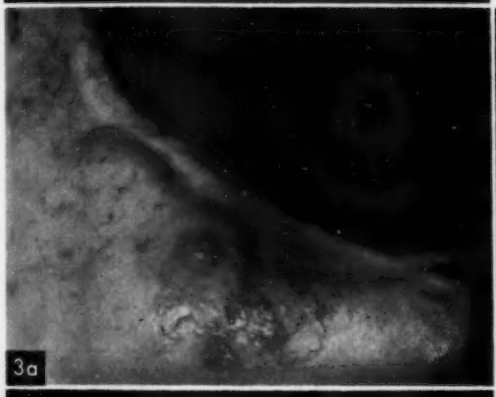

TABLE 2

TREATMENT OF INFECTED ECZEMA

1. Avoid all irritation, particularly from medications
2. Cleansing—Soap and water when tolerated
3. Dryness—Avoid occlusive dressings
4. Debridement of dead tissue, incision and drainage of pus when present
5. Topical antibiotics (following cultures and sensitivity tests)
6. Systemic antibiotics if fever, chills, adenopathy, cellulitis or other signs of systemic involvement are present
7. VIOFORM® 3 per cent cream applied t.i.d. or q.i.d. after compressing
8. Soaks and compresses (silver nitrate 0.1 to 0.25 per cent aqueous solution, potassium permanganate 1:16,000 to 1:32,000, Dalibour's solution 1:20 to 1:40), 20 minute soaks every two hours
9. Rest, sedation and tranquilization when indicated

3. Mycotic Eczema

The clinical diagnosis of fungous infection of the hands frequently is made on insufficient evidence. A culture and a smear are mandatory. Dermatophytosis probably accounts for less than 2 per cent of all cases of hand eruptions. It is seen most frequently in young adults during the summer months.

There are three main types of mycotic hand eczema: the inflammatory type, the chronic type, and interdigital monilial infection.

Inflammatory type (Trichophyton gypseum)—This organism produces a vesicular, usually unilateral eruption affecting the palms and the sides of the fingers and occasionally the web spaces and nails. The eruption is erythematous, patchy, pruritic and sharply marginated, and the trichophytin skin test is positive. Pyogenic infection is a frequent complication.

Chronic type (T. purpureum)—This is a unilateral, usually noninflammatory eruption of the palms and the dorsa of the fingers. There are no vesicles. The lesions are dull red in color, sometimes become fissured, and usually develop a fine scale on their surface. Central clearing is absent, there may be severe pruritus, and sweating is diminished in the area of the lesions.

Interdigital monilial infection (Candida albicans)—Fissures on a red base develop in the interdigital web spaces, usually between the third and fourth fingers. They have a moist surface and a peeling, overhanging border. They are nonpruritic but may be very tender. Onychia and paronychia may be seen in the same patient (plate 2). The condition is partially occupational in origin, as exposure to water, irritant soaps and alkalies is an important predisposing factor.

Treatment of mycotic eczema of the hands is summarized in table 3.

4. "Id" Eruptions

An "id" represents an allergic reaction to the products of an eruption disseminated to a distant site. The products are borne to the area of the "id" via the blood. Although the mechanism of "id" eruption is invoked in cases of bacterial infection ("bacterid") or even simple eczema, the term is used most frequently in connection with fungous infections. "Id" eruptions are relatively uncommon; they sometimes occur after overtreatment or acute exacerbation of tinea pedis.

Dermatophytid eruptions are bilateral, involving the palms and the sides of the fingers with a pruritic, erythematous, vesicular eczema. In a sense the hands, though uninfected, mirror the tissue's reaction to the organism at the distant site. As the primary focus is elsewhere, the lesions heal when the original area improves.

Cultures from lesions of "id" eruptions are sterile. In a true dermatophytid eruption the

TABLE 3

TREATMENT OF MYCOTIC HAND ECZEMA

1. Soaks and compresses for 20 minutes five to six times daily (Dalibour's solution, $KMNO_4$ 1:16,000, boric acid solution), cool or at room temperature
2. Debridement of hypertropic areas
3. Castellani's paint applied to fissures
4. Avoid moisture and maceration; keep skin dry between soakings
5. Anticholinergic medications to reduce perspiration (Pamine, 2.5 mg. two to three times daily, or Pro-Banthine, 15 mg. two to three times daily)
6. Rest and sedation, avoidance of continued irritation
7. Antifungal agents: ammoniated mercury, undecylenic acid, MYCOSTATIN® ointment and powder (the last-named agent is used for moniliasis only)

trichophytin intradermal skin test will be positive and fungi can be recovered from the primary focus of infection (plate 3). A positive trichophytin test alone, however, does not necessarily indicate an "id" eruption but merely denotes the presence of previous sensitization by a fungus.

Table 4 outlines the treatment of "id" eruptions.

5. *Nummular Eczema*

Nummular eczema is so named because the lesions resemble coins (plate 4). There are discrete erythematous plaques studded with papules and vesicles which progress to exudation. Lesions are sharply marginated, without a raised border, and ooze from numerous small points, leading to secondary crusting. These coinlike plaques are highly pruritic, recalcitrant and recurrent, and central clearing occurs as they enlarge. The dorsa of the hands and fingers and the extensor surfaces of the forearms and arms are most commonly affected, but lesions may also appear on the legs, thighs and shoulders. Nummular eczema reaches a peak during the winter months. Psychic stress and a dry, asteatotic skin are frequent components of nummular eczema.

Although the disease has been accurately described for many years, its bizarre nature has stimulated variable views as to its etiology. In one large series of cases an atopic background was indicted. Another author concluded that asteatosis resulting from vitamin A deficiency was the primary factor. Others have called nummular eczema a variant of dermatitis herpetiformis, a form of bacterial allergy, and a disturbance of function of the cutaneous nerves. We believe nummular eczema has multiple causes and is not a single distinct entity (figure 6). The cause or causes are unknown but many contributing factors are recognized. The term "nummular eczema" should remain a purely descriptive one.

Table 5 outlines the treatment of nummular eczema.

TABLE 4

TREATMENT OF "ID" ERUPTIONS

1.	Avoid treating the eruption actively
2.	Astringent soothing compresses or soaks to the hands (boric acid solution, Dalibour's solution)
3.	Bland creams or simple ointments
4.	Protection of hands from trauma (cotton gloves)
5.	Avoid excessive moisture and maceration
6.	Treat primary fungous infection but avoid overtreatment, which will aggravate and intensify the "id"
7.	Decrease hyperhidrosis by rest and sedation, and anticholinergics (Pamine, 2.5 mg., or Pro-Banthine, 15 mg.)
8.	Cortisone or corticotropin therapy for severe cases only

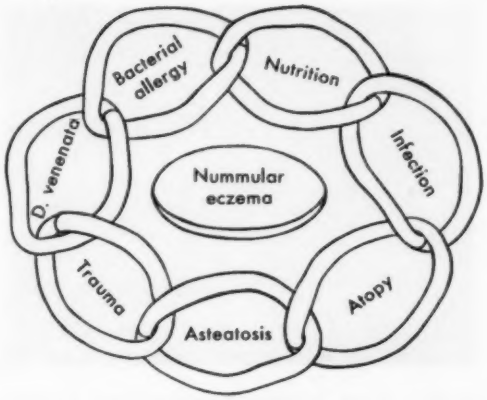

FIGURE 6. Diagram showing complex chain of possible etiologic factors in nummular eczema.

TABLE 5

TREATMENT OF NUMMULAR ECZEMA

1.	Antipruritic soothing compresses ($KMNO_4$ 1:32,000, silver nitrate 0.1 per cent solution)
2.	Sedation
3.	Antihistamines for pruritus
4.	Treat secondary infection (antibiotic creams)
5.	Topical therapy (crude coal tar often successful)
6.	Vitamin A supplement may help
7.	Emollients to correct excessive dryness (petrolatum, ALBOLENE®, Lubriderm, Oilatum cream)
8.	Avoid hot water, soap, detergent; infrequent bathing recommended
9.	Ultraviolet light therapy
10.	Topical steroid therapy usually disappointing

6. *Pompholyx*

Pompholyx was first described in 1871 by Sir Jonathan Hutchinson. The cause is still unknown. Although the terms "pompholyx" and "dyshidrosis" frequently are used synony-

FIGURE 7. Atopic dermatitis of hands. Patient also had atopic dermatitis elsewhere.

TABLE 6

TREATMENT OF POMPHOLYX*

1. Control hyperhidrosis
2. Keep hands dry
3. Avoid trauma to skin
4. Rule out foci of infection
5. Apply 3 per cent salicylic acid in isopropyl alcohol p.r.n.

*No specific approaches are of value; measures suggested for palliation.

mously, they are not the same. Dyshidrosis is a generic term and denotes any derangement or abnormality of the perspiratory apparatus —hyperhidrosis, hypohidrosis, bromhidrosis or chromhidrosis.

In pompholyx an eruption is seen on the palms and the sides of the digits consisting of fine, deep-seated vesicles resembling sago grains (plate 5). Its appearance often leads to a mistaken clinical diagnosis of "id" eruption. There is no erythema associated with the vesicles, and they do not rupture but resolve, leaving only a fine, delicate scale. The condition is recurrent. It is aggravated or triggered by emotional tension and is worse in hot weather, when hyperhidrosis may be a coexisting and aggravating factor. Recent histologic studies have shown clearly that the vesicle of pompholyx does not arise from or depend on blockage of the sweat ducts, as was formerly believed. The term "dyshidrosis" applied to pompholyx is a misnomer.

TABLE 7

TREATMENT OF ATOPIC HAND ECZEMA

1. Treatment varies with extent, stage and degree of eruption
2. When acute, use wet compresses and soaks
3. When infected, use topical antibiotics
4. Antieczematous agents (tar, 2 to 5 per cent; ichthammol, 3 per cent in zinc oxide ointment)
5. Sedation and tranquilization
6. Steroids and foreign protein therapy (symptomatic benefit only)
7. Topical corticosteroids (palliative value)
8. Hyposensitization regimens of doubtful value

There are no specific therapeutic approaches of value in pompholyx. The measures outlined in table 6 are suggested for palliation.

7. Atopic Dermatitis

It is well known that atopic dermatitis often involves the hands. However, atopic dermatitis confined to the hands is rare. The clinical features are well established and constitute a characteristic syndrome. The lesions usually localize to the face, neck, antecubital spaces and popliteal fossae. It is a syndrome that has variations in its natural history.

In considering the diagnosis of atopic dermatitis in a case of eczema of the hands one must first determine the presence of atopy. Personal and family histories should be obtained. Atopic dermatitis is aggravated by extreme heat, cold, humidity, infections and emotional upsets. White dermographia may be demonstrated. Eosinophilia and immediate wheal reactions occur in atopic persons.

In atopic eruptions of the hands the important aggravating factors are topical overtreatment, soaps, wool, sometimes silk, retention of sweat, and emotional upsets. Information from standard scratch and intradermal tests is of little value. In any discussion of atopic dermatitis of the hands one must emphasize the complex pattern of the syndrome of atopy with its highly variable course (figure 7). The treatment of atopic eczema of the hands is outlined in table 7.

8. Food Allergies

There has been considerable interest in the subject of foods in relation to eczematous

eruptions of the hands. The alleged eruptions from foods are not distinctive and are said to resemble dermatophytids, bizarre eczematoid contact dermatitis, or vesicular neurodermatitis. The lesions described appear on the dorsa of the hands, particularly about the wrists, and are dry, nonvesicular, lichenoid and roughly circular. As in many other eczemas of the hands, the condition is aggravated by soap, gross infection or by psychic stress.

Foods indicted have been milk, wheat, eggs, pork, tuna, coffee, asparagus, peas, apples, tomatoes, chicken, nuts and grapefruit, the first four most commonly. Investigation of possible food allergy is fraught with difficulty and pitfalls. If one suspects food allergy in a patient with chronic vesicular eruptions (particularly an atopic patient), one must first eliminate other possible causes. Ideally, the patient should be hospitalized. Following removal of the offending allergen (food?) there should be improvement. When the substance is again ingested the condition should become worse within 24 hours. Unfortunately this sequence of events cannot always be attributed to food ingestion, for other factors play a part. Although food allergy may be suspected in cases of chronic vesicular eruptions involving the hands, particularly in atopic persons and those with unexplained vesicular relapse or exacerbation after contact factors have been eliminated, it probably represents an *extraordinarily uncommon* cause per se of dermatitis of the hands.

FIGURE 8. Acrodermatitis continua. Persistent recalcitrant pustular eruption involving the tips of the fingers.

FIGURE 9. Pustular psoriasis. Crusted areas of sterile pustular lesions in palmar distribution.

9. Inhalant Allergies

Cases have been reported incriminating inhaled allergens, particularly air-borne molds, ragweed pollen and the pollen of grasses or trees, as sole factors in hand eczema, but such cases are rare and hard to prove. The lesions are bilateral and symmetrical, on the dorsa of the hands or knuckles and the dorsa and sides of the fingers. The palms and wrists usually are spared. Antigenic inhalants such as house dust, wool, feathers, silk and danders may be aggravating factors in atopic persons. Seasonal exacerbations are frequent and there usually is an associated "asthma-rhinitis" complex. Eczemas from allergies to animal emanations, dust and tobacco also have been described. Diagnosis is based on history (exposure and season), positive results with skin scratch testing, and good results from a program of hyposensitization.

10. Miscellaneous Hand Eczemas

There remains a group of rather uncommon conditions affecting the hands which should be mentioned. Lichen planus palmaris, perniones, pellagra, acrodermatitis continua and dermatitis repens have characteristic features (figure 8). The clinical picture is also quite typical in seborrheic eczema, early dermatitis herpetiformis and psoriasis (figures 9,

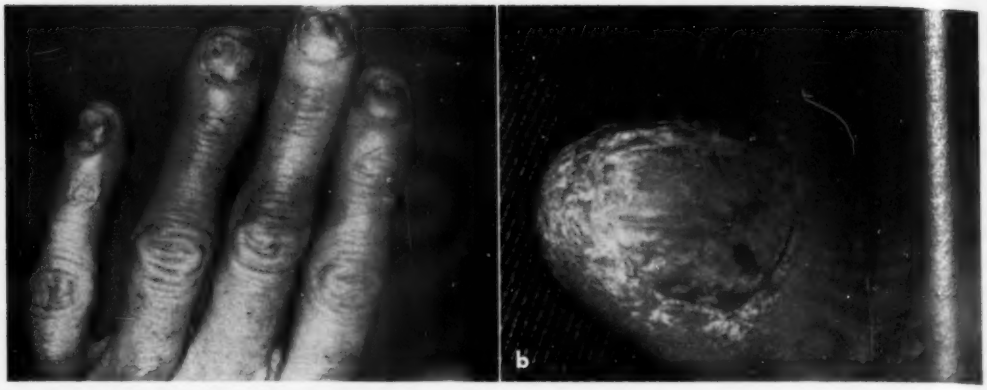

FIGURE 10a and b. Psoriasis involving the nails.

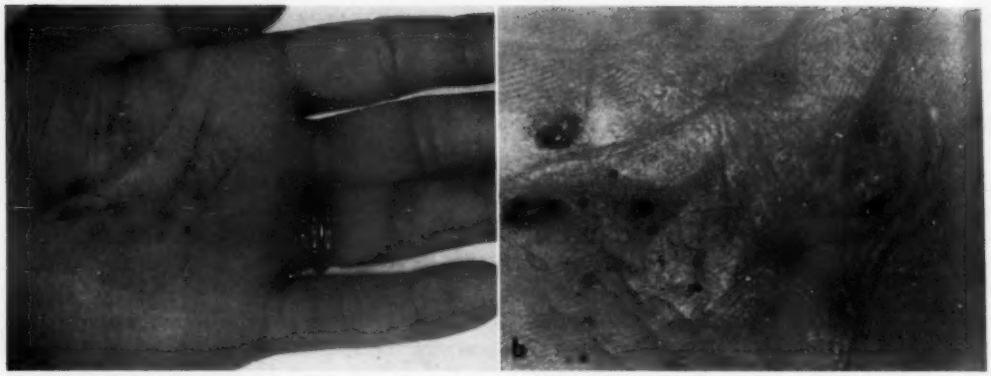

FIGURE 11a. Dermatitis factitia. Lesions simulating chronic hand eruption produced by patient with sharp object. (Litigation case.) b. Close-up of same.

10 and 11). Parasitic infestations, such as scabies, and "fixed" drug eruptions may involve only the hands. The persistence and resistance of many cases of eczema of the hands frequently are caused by the insidious influence of chronic irritation, trauma and overmedication.

Conclusions

In the study of any case of eczema of the hands one should bear in mind the importance of secondary factors. These may be responsible not only for the development but also for the persistence of the lesions. The most common offenders are soaps, infections, psychic stress, atopic background, aggravation by treatment, heat, hyperhidrosis, and secondary autoeczematization.

Since inspection and history alone often fail to reveal the cause of eczema of the hands, laboratory aids frequently must be invoked. Most helpful may be the following procedures: (1) bacteriology (culture, sensitivity, smear of the lesion), (2) pathology (biopsy of the skin), (3) mycology (potassium hydroxide mount, culture and trichophytin skin test), (4) patch testing, and (5) hematology (anemia, eosinophilia, leukocytosis).

Summary

An attempt has been made to describe the plurality of etiologic factors, and the frequency

of "vicious cycles," in the causation of hand eczemas. An understanding of this is helpful in elucidating the causative agents and directing therapeutic approaches toward a specific program. The classification of hand eczema into 10 major groups provides a rational approach to specific diagnosis and therapy.

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Coming next in this series on Diseases of the Skin

Acne — the Situation at Present

by HERBERT RATTNER, M.D.

Professor and Chairman, Department of Dermatology,
Northwestern University Medical School, Chicago

Physicians must keep well abreast of current developments in drug therapy to provide adequate and proper treatment of cardiac conditions. From his own experience, the author reviews the use of digitalis, rhythm-regulatory drugs, coronary dilators, cardiac stimulants, diuretics, antihypertensive agents and anticoagulants. He cautions that older therapeutic agents should not be discarded until the newer ones have been proved effective.

Effective Cardiac Drugs

ARTHUR C. KERKHOF*

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PROPER and effective treatment of cardiac disease requires an accurate knowledge of drugs in several classifications. Unfortunately, many practitioners of medicine find their information concerning these drugs inadequate and seek additional information from questionable sources. They are particularly prone to accept statements from those who are promoting specific medications. It is easy to understand how difficult it is for the average physician to keep abreast of all the expanding and accelerating phases of medicine, but one area in which he must keep current involves drug therapy. The conscientious physician is extraordinarily susceptible to any talk about new drugs, and because he does not wish to appear old-fashioned he indiscriminately uses new drugs to show that he is keeping up with modern medical trends. This nearly universal tendency undoubtedly has led to inadequate and sometimes improper therapy of cardiac conditions.

ARTHUR C. KERKHOF

I shall present some observations on the nature and effect of drugs I have personally used during my practice of cardiology, which now embraces more than 20 years. In a brief summary such as this it is clearly impossible to discuss each drug, so I will talk about various categories and give a few examples in each.

Digitalis

Digitalis, one of the oldest known cardiac drugs, even today is not always used correctly. Preparations of the drug vary from the crude drug itself to a very finely crystalline product, but the general principles underlying their use are the same. Digitalis tends to decrease the length of the muscle fiber, thereby increasing its efficiency and also decreasing the oxygen requirement of the heart muscle, which in turn means increased efficiency. It must be used properly to obtain this result.

Going back to the original work of Eggle-

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Presented before the forty-third annual Assembly of the Interstate Postgraduate Medical Association at Cleveland.

ston, who first standardized the use of digitalis, you will recall that the drug at that time was standardized by the cat unit method. Eggleston found that in the average person the peak of digitalis effectiveness was reached when 1 cat unit per 7 lb. of body weight was administered. The curve representing the increased efficiency of the heart muscle rises abruptly after the first few units are given and finally stabilizes on a very slowly rising plateau. If we were to use the value of 1 cat unit per 7 lb. of body weight we would find that, while we were correctly digitalizing the average person, certain patients would be overdigitalized and have toxic signs from the drug. Still others would not be completely and fully digitalized for they would be on this plateau which precedes full digitalization.

Overdigitalization decreases the efficiency of the heart muscle markedly, because even in minute degree it causes the heart muscle to lose all the increased efficiency it previously gained from the digitalis. In some cases overdigitalization may even cause the heart muscle to have less efficiency than it did before digitalis was administered. Because of this factor with its consequent effects, Eggleston advocated the use of 1 cat unit per 10 lb. of body weight in order to avoid overdigitalization. This is still an excellent standard for digitalization and is quite properly used today.

A cat unit obviously varies from drug to drug. In digitalis leaf, 1.5 gr. could represent a cat unit, while in some other brand of leaf 1 gr. might be a cat unit. In some of the semipurified brands 1.5 gr. becomes a cat unit. In the crystalline form of the drug approximately 0.1 to 0.15 mg. is equivalent to a cat unit.

I prefer the slower-acting semipurified form of the drug unless there is an extreme urgency in its use. In a situation which is not acute I probably would digitalize a 150 lb. man over a week's period, giving him 3 cat units a day for one week, or 21 cat units in seven days; this total is based on the patient's losing 6 or 7 cat units through daily loss of the drug. He then would be maintained on 1 cat unit a day. For nearly all patients this schedule provides adequate digitalization, and 1 cat unit a day generally maintains most persons. Occasionally a patient requires up to 10 cat units a week for maintenance, while others require only 5 cat units.

If the situation appeared more urgent I might digitalize the patient in two days or even one. I would give the total of 15 cat units over that period, plus 1 cat unit a day for each additional day used in digitalization. After that I would maintain him on 1 cat unit each day.

At times it is necessary to use intravenous medication, and there are several excellent products for this. CEDILANID® is one of the better intravenous preparations and it also may be given orally. The average 150 lb. man will be digitalized by 8 cc. of Cedilanid intravenously. The effect is felt in about one-half hour and reaches its maximum in about two hours. A maintenance dose is 2 cc. a day intravenously, or one-fourth the digitalizing dose. For oral administration, both the digitalizing dose and maintenance dose are the same as those for intravenous administration.

Since one-fourth of the digitalizing dose is required for maintenance when Cedilanid is used, digitalization ranges from 100 per cent one morning to 75 per cent the next morning just prior to administration of the maintenance dose. With the semipurified product the daily variation is only around 7 per cent, inasmuch as the maintenance dose is only one-fifteenth of the digitalizing dose.

DIGOXIN® is another recommended preparation for fast intravenous digitalization. Dosage is 1 mg. intravenously with a maintenance dose of 0.25 mg. daily. Thus the use of this drug also has the disadvantage of requiring an extremely high percentage of the digitalizing dose for maintenance.

When I have felt it necessary to digitalize intravenously I have used either Cedilanid or Digoxin and then changed over to one of the semipurified or crude products for oral use. When this is done I might digitalize a person intravenously with either Digoxin or Cedilanid and the next day start giving him one-fourth of the digitalizing dose of the oral preparation each day for four days. Under these circumstances he loses one-fourth of the digitalizing dose of the fast-acting drug and gains one-

fourth of the digitalizing dose of the slower-acting drug each day. At the end of four days he still has 100 per cent digitalization, and he is then maintained by the slower-acting drug, 1 cat unit a day.

My predilection for the products mentioned is based on my satisfactory experience with them personally, and in mentioning them by name I do not mean to exclude the many other fine digitalis preparations on the market. My statements should not be considered a blanket endorsement of these drugs to the exclusion of others, but merely represent my own opinion, which others may not hold.

In using digitalis one must also remember that if digitalization becomes necessary in a case of acute cardiac infarction it is wise to administer only two-thirds or three-fourths of the digitalizing dose, thus decreasing the chance of increased cardiac irritability and possible paroxysmal tachycardia. It is well known that overdigitalization carries with it the production of ventricular premature beats. In persons who already have this very hypersensitive myocardium, the effect of digitalis might suffice to produce ventricular paroxysmal tachycardia or ventricular fibrillation.

The primary indications for the use of digitalis are cardiac failure with increased heart size and, occasionally, an arrhythmia such as auricular fibrillation or auricular flutter without heart-failure. Some workers feel strongly that increased heart size itself is a cardiac failure even though congestive failure has not appeared, and that patients with increased heart size should be digitalized empirically.

Rhythm-regulatory Drugs

In cases of cardiac irregularities such as paroxysmal tachycardia, auricular fibrillation, auricular flutter and, occasionally, premature beats, drug therapy often is required in an attempt to restore normal rhythm. The drug chosen depends to a great extent on the type of arrhythmia.

In the most common irregularity, ventricular premature beats, quinidine or procaine amide generally will prevent the premature contraction. Both drugs decrease the irritability of the ventricle, procaine amide to a lesser extent than quinidine. For this condition I would rather use quinidine, giving it in a dosage of 3 gr. tablets three or four times a day along with a mild sedative such as phenobarbital. In most cases this combination of drugs will restore normal rhythm and thereby reassure the patient. This reassurance actually is more important than the restoration of normal rhythm. I frequently prescribe these drugs for a patient merely to prove to him that the premature beats can be prevented, and eventually he realizes that the daily taking of drugs is worse than the discomfort the premature beats may cause. It is, after all, commonly accepted that ventricular premature contractions most often are a result of nervous influence and not of any cardiac abnormality. However, in acute myocardial infarction, in certain infectious forms of myocarditis, and in instances of overdigitalization they are a direct result of an effect on the myocardium itself.

The drug to be used in paroxysmal tachycardia depends on the location of the focus. In auricular paroxysmal tachycardia the most effective drug is digitalis in normal digitalizing doses. MECHOLYL® can be used, but its side effects rapidly discourage the average physician from prescribing it. In auricular paroxysmal tachycardia with block, digitalis is not to be used. Potassium usually will stop this arrhythmia. Nodal paroxysmal tachycardia is very effectively treated at times with digitalis but will also respond to quinidine.

In my opinion either procaine amide or quinidine sulfate is an effective therapy in ventricular tachycardia. Except under very rare conditions, digitalis is not to be used in paroxysmal ventricular tachycardia; the exception here proves the rule. Remember that digitalis itself tends to produce ventricular irritability, and ventricular paroxysmal tachycardia is a sign that ventricular irritability already is increased. The intravenous administration of 800 to 1000 mg. procaine amide in 150 to 200 cc. of fluid is a very effective treatment and usually produces prompt cessation of the paroxysmal tachycardia. If the blood pressure is low, LEVOPHED® must be used and may stop the arrhythmia by itself. Quinidine given by mouth has been very successful

as I have used it. Usually one gives the patient a 3 gr. dose and then waits an hour or so to rule out any possible severe toxic symptoms. Assuming that nausea, vomiting or collapse phenomena do not occur, the patient is then given 3 gr. an hour for two hours. If this is not successful, 6 gr. an hour is then given for three hours in an attempt to stop the abnormal rhythm. At times it is necessary to give 9 gr. an hour for three hours, and rarely dosages as high as 85 gr. in four or five hours are necessary. Certainly by this time the physician should have no fear concerning quinidine, for in itself it is not dangerous. Used correctly, it is a very effective tool in the treatment of cardiac disease.

Unless the ventricular rate is slow, auricular fibrillation usually requires a combination of drugs. If the rate is slow, quinidine can be used in an attempt to regulate the rhythm. I have not been particularly successful with procaine amide in this situation. Again the patient is tested with a 3 gr. dose of quinidine. The next morning he is given 3 gr. an hour for three hours, at 8, 9 and 10 o'clock. If the rhythm does not become regular that day, the total daily dosage is increased by 3 gr., giving him 6 gr. at 8 o'clock, 3 gr. at 9 o'clock, and 3 gr. at 10 o'clock. If the rhythm still does not become regular, the daily dosage again is increased so that he takes 6 gr. at 8 o'clock, 6 gr. at 9 o'clock, and 3 gr. at 10 o'clock. This slow increase in dosage is continued until the patient receives 12 gr. at 8 o'clock, 9 gr. at 9 o'clock, and 9 gr. at 10 o'clock. If the rhythm does not become regular with this schedule, our experience has shown that it is impractical to attempt to regulate it. Even though higher doses of quinidine might regulate the rhythm, it would be impossible to maintain such regularity by ordinary maintenance doses of quinidine.

Assuming that this gradually increased schedule of quinidine administration does regulate the rhythm, the dosage is then gradually decreased until the patient receives 3 gr. four times a day and finally 3 gr. three times a day, on which dosage he is maintained for an extended period.

If the ventricular rate is fast, and particularly if auricular fibrillation has been present for some time, digitalization is very helpful in obtaining regular rhythm. The patient should be digitalized in the manner already outlined, and quinidine should be used according to the schedule presented. There is no reason the two drugs cannot be used simultaneously, for they are entirely compatible.

The same drugs would be used for auricular flutter as for auricular fibrillation. The method is practically the same except that the dosage of digitalis is increased to produce a marked block between the auricles and ventricles and then quinidine is used in an attempt to restore normal rhythm. Occasionally digitalization in itself restores normal rhythm in both auricular fibrillation and auricular flutter. However, auricular flutter is much more difficult to regulate than auricular fibrillation, and failure in such regulation is not necessarily a reflection on the physician's ability.

Coronary Dilators

The field of coronary dilators is particularly confused and perplexing these days, and new drugs appear perennially. As a practicing cardiologist I have found it most difficult to find a number of effective coronary dilators. Nitroglycerin is still the drug par excellence. Whenever there is anginal pain it can be used sublingually in doses of 1/200 gr. or 1/100 gr. in an attempt to relieve the angina. It is most effective in relieving angina pectoris, and no other drug is a comparable substitute. From my experience, there is no limit on the amount of nitroglycerin a person can take in one day. I have a patient who has taken as many as 150 nitroglycerin tablets a day without ill effect. The drug does produce a slight pounding in the head, but this is not serious and the patient is quite willing to accept it in return for relief of the angina.

Another use for nitroglycerin is to prevent anginal attacks. Many patients of mine who know that a three or four block walk will precipitate angina pectoris will put a nitroglycerin tablet under the tongue before their stroll and experience no discomfort whatsoever. Nitroglycerin is therefore an effective coronary dilator to relieve angina pectoris but may also

be used in the prevention of angina pectoris.

Aside from nitroglycerin I do not know of any oral coronary dilator with any degree of effectiveness. Even though the drug markets are flooded with such preparations today, I personally do not know of any which I could unequivocally say has done my patients any good. Various drugs such as aminophylline and PERITRATE® have not been effective by mouth in any of my patients. Aminophylline is effective intravenously but it occasionally drops the blood pressure quite markedly, and the intravenous route is not practical for the average patient. Aminophylline given rectally in the form of a suppository can produce effective coronary dilation, but, unfortunately, patients cannot endure this therapy long because of the proctitis which usually occurs.

Cardiac Stimulants

In my opinion one of the weakest areas of modern drug therapy is the field of cardiac stimulants. By this I mean the direct stimulation of cardiac musculature. CORAMINE® has been used many times to revive patients who need resuscitation. I have not found it to be an effective long-term drug. Coramine can be given intravenously, and intracardially if necessary, but aside from an acute emergency it will not prove effective in the long run. Oxygen itself is a cardiac stimulant in a sense, because increased oxygen in the arterial blood will increase oxygen in the heart muscle and therefore suffice to tide the patient over certain situations.

ADRENALIN® administered intracardially has been used in cases of Adams-Stokes syndrome where ventricular standstill has occurred. However, it can be a dangerous drug if, for example, the attack is not a cardiac arrest but actually ventricular fibrillation; in this situation the Adrenalin would only serve to aggravate the condition.

Diuretics

Diuresis is an important part of the therapy of congestive heart-failure. There are many forms of diuretics available. Ammonium chloride given orally, 15 gr. three to four times a day, will tend to acidify the urine and thereby increase the output of water and sodium. Mercurial diuretics given intramuscularly or subcutaneously decrease the concentrating ability in the tubules of the kidneys, thus producing a very dilute urine with a marked increase in urinary output. A combination of ammonium chloride and the mercurials is very effective.

Recently DIAMOX® has been used for diuresis. It increases the output of sodium bicarbonate and consequently aids in eliminating large amounts of water which were held in the tissues by the sodium. DIURIL®, another of the new diuretics, markedly increases the output of sodium, producing diuresis, and also decreases the blood pressure. Unfortunately, large amounts of Diamox can produce a very definite acidosis. When it appears that a patient has dyspnea without crepitation in the lungs and without other signs of congestive failure following the use of Diamox, it behooves the physician to check the carbon dioxide-combining power to see whether or not acidosis with resultant acidotic breathing has occurred. On the other hand, Diuril has sometimes produced alkalosis, and this condition must also be watched for when that drug is used. It also causes a loss of potassium which must be corrected. As far as I can see, there is no contraindication to the use of any combination of these drugs at the same time in the same patient. Each has its own place in the therapeutic armamentarium, and the combined effect, although quite possibly not equal to the sum of the individual effects, at least is more than the effect of any one drug.

Digitalis is also a diuretic in a sense because it increases cardiac efficiency and thus decreases venous pressure. There is less tendency for water to go into the tissues and to form edema, and therefore more of it reaches the kidneys to be eliminated.

Antihypertensive Agents

For many years attempts have been made to treat hypertension with drugs. Thiocyanates were among the earliest ones tried, and they were used empirically because an adequate explanation of their actions could not be found. It is now becoming evident that thiocyanates cause a decrease in the lipoid content of the

adrenal cortex, and this suggests that one of the effects is to reduce the effectiveness of the adrenals. It has also been well demonstrated that sympathectomy increases the effects of thiocyanate on the adrenal cortex, and this leads to the possibility that a combination of thiocyanate and sympathectomy might prove quite effective.

Therapy with potassium thiocyanate is relatively simple but does require fairly regular determination of blood levels to avoid a rise to a toxic level. Blood levels up to 10 or 11 mm. per cent are perfectly safe, but higher levels can precipitate toxic symptoms. The drug has a sedative effect and will relieve headache, but once again a note of caution should be struck, for stupor can occur when toxic levels are reached. The infrequent thiocyanate goiter may be indicated by an enlarged thyroid, facial swelling, myxedema and so on, and can prove troublesome, but in my experience such a condition will disappear in six to eight weeks after the drug has been discontinued. Occasionally, but quite infrequently, a skin rash will occur with the use of this drug. Sometimes a secondary anemia will develop, but this will also disappear after the drug is stopped. Despite all the disadvantages of the drug, it will still produce a satisfactory drop in blood pressure as well as quite a marked decrease in the amount of headache in a considerable number of patients. It should not be used routinely in cases of the severe grades of hypertension.

In the past, ergot and various derivatives of that drug were tried for treatment of hypertension. Although there have been optimistic reports on their use, I mention them only because at present I see no great value in their use in treatment of hypertension.

Veratrum has been used and is advocated by many workers. Nausea and vomiting frequently accompany its use, and the hypotensive dose is very near the toxic dose. Also, it appears that some persons develop a tolerance to the drug and its hypotensive effect wears off, whereas others may suddenly become quite highly sensitive to it and toxic signs may appear, even acute collapse. The results obtained with this drug vary with the investigators. Some claim a definite drop in systolic and diastolic pressure can be obtained and maintained, while others are unable to achieve such results. Those who do claim decreases of pressure also state that changes in cardiac size and in the eyegrounds occur, but it is well known that any therapy which reduces severe hypertension will result in similar changes. One of the derivatives of *Veratrum*, called protoveratrum, recently has been used with favorable results, but again the margin between toxic and therapeutic levels appears dangerously narrow. I do not believe it is a drug to be used alone, for I doubt if one could get adequate results with the drug used in that manner. It may be useful as an adjunct to another form of therapy in reducing blood pressure.

Tetraethylammonium drugs also must be mentioned in a discussion of drug therapy of hypertension, but because of the marked drop in blood pressure they produce at times and because of the rather short duration of effect they cannot be recommended for ordinary therapy.

Hexamethonium and allied drugs are probably the most powerful antihypertensive agents in clinical use today. They act on the sympathetic and parasympathetic ganglia. Side reactions are nearly all the results of the effect on the autonomic nervous system. Gastrointestinal symptoms, such as diarrhea or constipation, are quite common. Faintness and lassitude commonly accompany the marked drop in blood pressure. Hexamethonium can be given orally or parenterally. As one would expect, the hypotensive effect is more rapid when it is given parenterally. Oral administration produces a slower and longer effect.

I have used a considerable amount of ANSOLYSEN® orally in the past in an attempt to reduce blood pressure. At present I do not believe this drug meets a definite therapeutic need unless the blood pressure is extremely high. If I were to use it under these conditions I would start by giving the patient 20 mg. orally four times a day, taking the blood pressure just prior to administration of each dose of the drug; if the pressure had fallen markedly since the previous dose, the drug would

not be given. If this dosage was not successful, the amount could be increased to 40 mg. four times a day. Doses as high as 120 to 160 mg. four times a day are quite common. However, because of the very marked hypotensive effect, it is necessary to determine the blood pressure prior to each administration of the drug to avoid marked hypotensive effects. Under these circumstances it is quite common and perfectly acceptable to teach the patient or a relative to take the blood pressure reading.

I regret that as time has passed I have become progressively more and more disenchanted with this whole group of drugs. Unless a severe hypertensive state is present I am rather reluctant to begin their use. While it is entirely true that with them one can reduce blood pressure, often such a reduction in persons with very high values produces unfortunate side effects. One such effect is that the vascular system no longer is able to carry enough blood to supply the needs.

Hydralazine, known commercially as APRESOLINE®, is another hypotensive drug that may be used alone or in combination with other drug therapy. It may be given in doses of 25 to 50 mg. every four hours, gradually increasing the dosage to as much as 800 mg. per day. This drug acts on the so-called humoral aspect of hypertension and therefore is an adjunct to the other types of drugs. Apparently it will supplement the effects of hexamethonium and may help smooth out the blood pressure curve. It has also been used with *Rauwolfia* and its various derivatives. In my practice it has not proved to be a very successful drug, but in all candor I must admit that many other physicians have found it very helpful. Side effects include headache, tachycardia, dyspnea, paresthesias and mental depression.

The addition of *Rauwolfia* to the therapeutic armamentarium for hypertension held bright promise, for at first it was thought to hold the answer for all sorts of treatment riddles. It was fully predicted several years ago that when the first wave of enthusiasm had passed we would find it relegated to a more minor role, and this, of course, has come about, as any student of medical developments knew it would. The drug itself has a marked sedative effect and this, together with its relaxing effect, does tend to reduce blood pressure—albeit as a rule it is not a drug that is successful in extremely marked hypertension. Actually it should probably be used only in mild hypertension or for patients who need sedation. It may also be suggested for use in combination with other drugs in treatment of more severe hypertension.

The latest addition to the arsenal of antihypertensive drugs is Diuril. This drug is highly popular at present and does have a definite hypotensive effect. It is effective because it removes sodium in the urine and thus decreases the blood pressure. It seems to be very effective in many cases. Nevertheless, in the light of medical history we know that much of this enthusiasm will pass and it too will be relegated to a less prominent position as a drug for the treatment of hypertension. Dosage usually is 500 mg. once or twice a day. It produces fairly marked diuresis, as I have already stated, and also very definitely reduces the blood pressure.

Before leaving the drug therapy of hypertension it is necessary to issue a word of caution, and I offer it in a friendly, constructive fashion out of my own experience. I know the average physician is extremely concerned about patients whose blood pressures are slightly elevated. If we are honest with ourselves, we should admit that frequently we are treating blood pressure which actually falls within the normal range as established by reputable studies. Such treatment with hypotensive agents is of no avail to the patient except to reassure him and create a sense of emotional security. As long as the physician knows he is treating the patient's psychology rather than his blood pressure, such therapy is justifiable, but if he feels he actually is doing a very fine job by reducing the blood pressure he is only indulging in medical mumbo jumbo. These remarks do not apply to severe grades of hypertension, but the latter are uncommon and represent only a small number of the large group of patients being treated for hypertension. In my own practice I use only a few of these drugs. I still like to use potassium thiocyanate in cases in which headache is a marked symp-

tom. A patient who is psychically disturbed or emotionally upset does well with treatment with *Rauwolfia* derivatives. A patient who has some tendency to edema formation along with the hypertension will be a prime candidate for therapy with Diuril. Combinations of these drugs are used frequently. I cannot recall in my last year of practice an instance when I have prescribed such drugs as Ansolysen, *Veratrum* or hydralazine.

Anticoagulants

Another group of drugs deserving discussion are the anticoagulants. Although some valid controversy still remains concerning the necessity for anticoagulant therapy in the average case of coronary thrombosis, there certainly is no disagreement that the severe case of coronary thrombosis should be so treated. Maintenance of prothrombin times of approximately two to two and a half times the normal control prothrombin time seems definitely to decrease the number of thrombo-embolic phenomena after coronary thrombosis and consequently lowers mortality. For myself, I find it a difficult professional problem to decide which cases are "severe" and which are "average." Because of this, I find I am treating all my coronary thrombosis patients with DICUMAROL® if at all possible. I realize that certain circumstances contraindicate anticoagulant therapy, but as a rule I have had little difficulty with it.

There are many drugs in this category on the market today. I use Dicumarol, and the usual routine is to give 300 mg. the first day, 200 mg. the second day, and then try to maintain the prothrombin time somewhere between 22 and 28 seconds as against the normal control of 12 to 13 seconds. This is not too difficult. When the patient is ready to leave the hospital after a coronary thrombosis, it is a simple matter to add up the amount of Dicumarol given in the last 10 to 12 days and determine the daily average. We usually find that after this it is sufficient to take the prothrombin time every three weeks.

Statistically there appears to be some evidence that maintaining patients on Dicumarol following coronary thrombosis decreases the rate of recurrence. Obviously all recurrences cannot be prevented, and coronary thrombosis may occur while the patient is taking anticoagulants. For the past several years all our coronary thrombosis patients have been maintained on anticoagulant therapy and there has been almost no difficulty in maintaining their individual levels. Some patients have had a second coronary thrombosis despite anticoagulant therapy but most of our patients have had little difficulty.

Another interesting development concerns the use of Dicumarol as a therapeutic agent to decrease anginal attacks. Our practice shows that the establishment of a therapeutic prothrombin level with Dicumarol and maintenance of that level over a long period definitely decrease the number of anginal attacks. Whether this is because of a change in the viscosity of the blood or because of a change in the fat content of the arteries I do not know. I do know patients get along better and have fewer anginal attacks than when they are not taking the drug. The reassurance the patient has that this drug therapy has been known to reduce anginal attacks might also be responsible. We know anginal attacks frequently are emotionally motivated and one must keep in mind the distinct possibility that the success of this therapy may be due to a psychologic aspect rather than the actual effects of the drug. Suffice it to say, however, that if following this method makes my patients more comfortable and if they have fewer anginal attacks, I feel the use of this drug is justified.

Conclusion

I have not attempted to cover entirely the field of effective cardiac drugs. All the drugs in this field cannot be mentioned by name, and any singling out of a particular brand is not to be interpreted to mean that other brands of the same medication are not as effective. I have attempted to outline what has happened in my own practice. Therefore I have discussed the drugs I have personally used.

We in private practice would do well to heed the advice of a great teacher who advised his students, "Be not the first to try the new nor the last to cast the old aside."

Melanomas often occur on the feet and quite commonly on the genitals. An association between pregnancy and growth of melanomas has been noted. Suspicious-appearing moles in children should be removed before puberty. The author recommends wide excision of the tumor and surrounding skin and extirpation of adjoining lymphatics.

Moles and Melanomas

GEORGE T. PACK*

Cornell University Medical College, New York

ONE of the most baffling problems in neoplastic disease is that of the ubiquitous mole and the iniquitous melanoma. The mole is one of the most common of all tumors; the melanoma ranks among the cancers of relatively infrequent incidence. The mole is constantly available for study and the melanoma is the most accessible of all malignant tumors. The low curability of the malignant melanoma is a constant stimulus toward efforts at improvement: in prevention by excision of moles considered dangerous and by more radical surgical attack on the malignant tumors.

GEORGE T. PACK

One thousand adult patients who came to a general diagnostic clinic with no concern about their moles were examined to ascertain the distribution and character of their nevi, and a composite scattergram was made. This study revealed that the average patient had 15 moles and that such true nevi, as distinguished from pigmented spots, were relatively scarce on the feet and on the genitals. In a comparative scattergram showing the regional distribution of malignant melanomas in 1,225 patients, it was found that the melanomas were very frequently located on the soles of the feet and quite commonly located on the genitals. This was in contradistinction to the general distribution of pigmented moles. It may be concluded from this comparative analysis that there is apparently a greater hazard of certain moles occurring on the feet and genitals. The junctional nevi which are most inclined to become melanomas occur three times as frequently on the feet as on other skin surfaces. The lesson to be learned from such a knowledge is the advisability of surgical excision of such pigmented moles found in these locations.

With due consideration for the frequency of different complexions and racial types, it may be stated that malignant melanomas oc-

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cur most often in blond individuals, particularly those who have extremely pale, soft-textured skin, and including those with a sandy complexion or with red hair, who may freckle easily, but who do not tan well or heavily on exposure to sunlight. Our clinical impression has been that the prognosis is extremely bad in this type of person. So evident has the fact been to us in the study of this large group of patients, that we urgently advocate the routine removal of all brown or black moles in blonds or red-headed people of this coloration as a proper prophylactic measure. Simple surgical excision or excisional biopsy with primary wound closure is sufficient for moles that have the clinical appearance of benignity.

It has been our policy to advocate the removal of all moles of suspicious or dangerous character in infants or children, before the possibility of malignant transformation can occur. Such moles are generally removed before the advent of puberty to avoid the hormonal stimulation coincident with this state.

It is not always possible to observe by clinical means the transformation of a pigmented nevus into a malignant melanoma. When a pigmented mole has long been quiescent and then goes through certain changes, such as becoming elevated, with increasing pigmentation, or with ulceration, bleeding and localized discomfort or pain, it may indicate that the tumor is already malignant. When a pigmented nevus begins to bother the patient, it may signify that a melanoma has already developed. The local recurrence of a melanotic tumor or the appearance of metastases in regional nodes or distant viscera after conservative removal of a supposedly benign nevus indicates that the original tumor was already malignant but unrecognized as such at the time of the conservative excision. This offers a strong argument for routine microscopic study of every pigmented mole that is excised.

It has not been generally recognized that a malignant melanoma may have multiple primary foci in the same individual. Only 16 of our 1,250 patients with melanoma, however, have shown evidence of multiple primary lesions. The incidence is surely not great, but it is undoubtedly higher than is the frequency with which melanomas occur in the general population.

In studying the development of pigmented nevi, it is observed that many of these moles are not at all visible until after the onset of puberty. A child with a few scattered pigmented moles here and there may, in company with the endocrine changes attendant on the state of puberty, experience the rather sudden development of numerous moles on the skin of the face, trunk and extremities. There is one important type of pigmented nevus which bears such a close resemblance to malignant melanoma that it is not possible clinically to distinguish between the two. This type of nevus may be found in children from the age of one year to the time of puberty. Usually the nevus is darkly pigmented, bluish, blue-black or dark brown in color, smooth and well demarcated. When this tumor is excised and submitted to pathologists for diagnosis, the pathologists are sometimes unable to state whether the neoplasm is benign or malignant. Even though some of these tumors have structurally the conformation of the true melanoma, they ordinarily do not behave as such until after puberty. Others are identifiable microscopically as a melanotic tumor largely peculiar to childhood, running a relatively benign course and labeled as juvenile or prepuberal melanoma. There have been some isolated instances wherein metastases have occurred from a prepuberal melanoma occurring in childhood. The significant conclusion to be drawn from this observation is the obvious necessity for complete surgical removal of all dark, deeply pigmented nevi in children. It may be a serious mistake to delay this operation until some evident change has occurred in the appearance of the tumor, sufficient to cause worry, particularly if this change develops at the time of or shortly after puberty.

The transformation of benign moles to malignant melanomas, the rapidity of their growth, early dissemination, and low rate of curability during pregnancy have not been generally known. In our experience with many patients with malignant melanoma, we have found 32 patients in whom pregnancy was associated in some way with the growth of the

malignant melanoma. The outlook for the patient with melanoma occurring during pregnancy is not good. This fact serves to stress the great importance of examining pigmented moles in young women during the time of pregnancy and their removal if the moles show any suspicious signs of growth.

Surgical Treatment of Melanoma

Once the diagnosis of malignant melanoma is made by excisional biopsy and microscopic study, the surgeon must perform an extremely wide excision of the tumor and the skin that surrounds it. Cosmetic restoration is not as important as safety, which is afforded by wide and deep surgical excision. In the majority of instances, the removal of skin must be so great as to necessitate the immediate application of a skin graft. The excision should go so deep as to constitute a three-dimensional dissection, involving not only the skin but also the underlying fat and fascia overlying the muscles in order to extirpate the adjoining lymphatics in the neighborhood of the melanoma.

The best prognosis, of course, occurs when the malignant melanoma is widely excised by these methods before metastasis has occurred. It is not always possible to detect metastases in the early stage or to know by which of the vascular routes cells will be disseminated. Those malignant melanomas that seem to metastasize by way of the regional lymphatics are still amenable to surgical treatment, but those melanomas that early enter the blood vascular system will spread through venous channels; these patients will ultimately develop visceral metastases and hence are incurable.

The principle of excision and dissection in continuity for primary and metastatic melanoma can be applied when the malignant melanoma is so situated in the skin as to be relatively and closely adjacent to the first relay of lymph nodes. The principle includes removing an elliptical segment of skin to include the primary melanoma, the skin intervening between the melanoma and the axilla or groin or neck, and excision of the lymph node-bearing region, together with a wide dissection of the underlying fat and fascia down to and exposing the muscles over this area. The operation is completed by a radical dissection of the regional lymph nodes that may contain metastatic melanoma. The fascial dissection is much wider than the sacrifice of the skin. By this means not only the primary tumor and the first relay of metastases in regional nodes are removed, but the intervening lymphatics as well. This measure should check to some extent the great tendency for metastases to develop in the intervening tissues between the primary site and the regional lymph nodes. The application of this principle in the treatment of melanomas has been responsible for improvement in end results.

Unfortunately, sometimes the primary malignant melanoma is situated in the skin at a site remote from the regional lymph nodes that are involved by metastases—for example, a melanoma on the sole of the foot with metastases in the femoral and inguinal lymph nodes, or a melanoma occurring in the nail matrix of the hand with metastases in axillary lymph nodes. With such an enormous intervening distance between the primary melanoma and the metastases in regional lymph nodes, it is not at all possible by any technical procedure to remove both primary and metastatic foci with the dissection of all the intervening lymphatics between the two sites. Yet there is a strong element of hazard in permitting any of the intervening lymphatics to remain.

Although the patient and the physician may immediately consent to such a radical operation as hip joint disarticulation for a sarcoma of the femur, it has been difficult to secure consent for this operation in the case of a small melanoma on the ankle with metastases to femoral lymph nodes; yet the disease is as fatal as other types of cancer that have more frightening aspects. Amputations for melanomas of the hands or feet with metastases to axilla or groin, respectively, require an amputation of the entire extremity plus dissection of the regional lymph nodes. The majority of such amputations have been performed late in the course of the disease when it is an operation of desperation or last resort, rather than an operation of election and hope. In occasional cases of primary melanoma on the hands and feet with metastasis to regional

nodes, axillary and groin dissections, respectively, have been successful, and the patients have survived for many years. These settings for this discontinuous procedure have been better than in the circumstances dictating amputation, but even here the great majority of patients have succumbed due to the recurrence of melanoma between the distal extremity and the site of node dissection. If amputations were done for melanomas of this more favorable distribution (only, of course, if metastases to axillary or inguinal nodes were proved) the end results might conceivably be better.

The New York Memorial Cancer Center series of patients with malignant melanomas shows continued improvement in end results of therapy by use of the therapeutic principles outlined. The five year definitive cure rate for all patients between the years of 1917 and 1945 was 21.4 per cent. The statistical department of Memorial Cancer Center has recently furnished us the end results of total experience covering all admissions to the Center, regardless of the stage of the disease, between January 1, 1948 and January 1, 1951; the five year definitive cures comprised 39.1 per cent.

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The success of treating varicose veins depends on the completeness with which the sites of valvular incompetency are interrupted. The pattern of valvular insufficiency and varicose veins varies greatly from patient to patient and must be assessed thoroughly before operation. To identify and localize valvular incompetency, the author recommends use of the retrograde leg-milking test, which he describes as a simple procedure that may be applied to all patients.

Assessment of Varicose Veins With the "Retrograde Leg-milking" Test

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THE basic anatomic defect in the pathogenesis of varicose veins is incompetence of the valves of the leg veins. Normally, venous valves in conjunction with the leg-muscle pump will direct the flow of the blood from the superficial veins to the deep veins and toward the heart (figure 1). Under conditions of valvular incompetency, blood tends to flow in a reverse direction, that is, from the deep veins to the superficial veins, whenever the patient is in the standing position. In addition, the leg-muscle pump becomes relatively less effective in propelling blood toward the heart during walking. Thus, failure of the venous valves and of the leg-muscle-pumping mechanism leads to increased peripheral venous pressure, stasis of blood, derangement of capillary function, hypoxia and chronic edema, ulceration, and other well-known pathologic and clinical manifestations of varicose veins. Ordinarily, varicose veins tend to be self-propagating, causing progressive dilatation of more distant veins and secondary changes of the skin and subcutaneous tissues.

Modern treatment of varicose veins involves the removal or obliteration, or both, of all abnormally dilated veins and the interruption of all accessible sites of valvular incompetency.[1] Currently, this is accomplished by ligating and stripping the greater (and often the lesser) saphenous vein and by ligating and dividing the incompetent communicating or perforating veins of the leg and thigh. The success or failure of this type of treatment depends on the completeness with which the sites of valvular incompetency are interrupted. If sizable shunts are allowed to remain, reflux of blood from the deep system to the superficial veins will continue, and some varicosities will remain or will recur.

Patients with varicose veins generally exhibit valvular incompetency in two primary areas:

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Presented before the forty-third annual Assembly of the Interstate Postgraduate Medical Association at Cleveland.

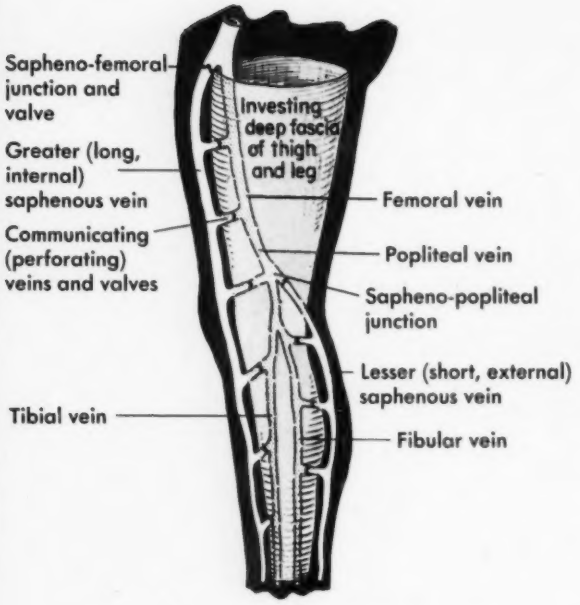


FIGURE 1. Principal components of the venous system of the lower extremity.

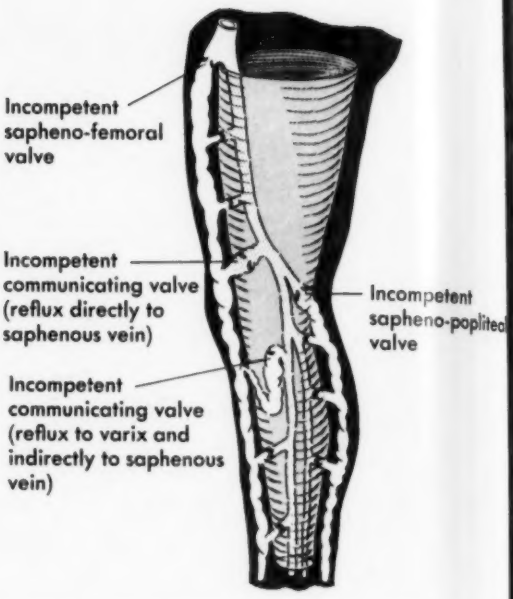

Incompetent sapheno-femoral valve
Incompetent communicating valve (reflux directly to saphenous vein)
Incompetent communicating valve (reflux to varix and indirectly to saphenous vein)
Incompetent sapheno-popliteal valve

FIGURE 2. Principal types of incompetent valves found in primary varicose veins.

(1) at the union of the main superficial trunks with the deep veins (the sapheno-femoral and the sapheno-popliteal junctions), and (2) the communicating veins of the leg and thigh (figure 2). Reflux at the sapheno-femoral valve can be demonstrated in some patients; some (about 10 per cent) will have reflux at the sapheno-popliteal valve, and many (about 80 per cent) will have one or more incompetent communicating veins.[2] The pattern of valvular incompetency (and varicose veins), therefore, varies greatly from patient to patient.

Many methods have been described for assessing valvular function in varicose veins. The most widely used tests are those of Trendelenburg,[3] Perthes,[4] Mahorner and Ochsner,[5] Schwartz,[6] Pratt,[7] Harkins and Schug[8] and Belcher.[9] Radiographic methods also have been recommended for localizing incompetent perforating veins.[10] In addition, certain physical signs have been described which may serve to indicate the site of perforator incompetency. These include the finding of isolated clusters of varices, the presence of palpable fascial defects near or beneath varices, and localized increases in venous pressure which can be detected by moving the finger along the course of the main saphenous channel.[11]

In the hands of those who use them constantly, the tests are extremely useful and give predictable results;[12] when used by the inexperienced, they leave much to be desired.[13] Too frequently, the conventional tests lead to confusion, slipshod application and little or no helpful information. Ultimately, the physician may conclude that the tests are unnecessary or are more trouble than they are worth, and he may treat the patient without having made a complete diagnosis. Under these conditions, the results of treatment generally will be unsatisfactory.

In assessing the patient with varicose veins, the need for a complete history and physical examination should be obvious. The importance of abdominal tumors, pregnancy and other causes of increased abdominal and venous pressure has been repeatedly emphasized. Likewise, one must suspect thrombosis of the deep veins of the leg from any cause when chronic edema, increased pigmentation

FIGURE 3. Varicosities of the greater saphenous system.

FIGURE 4. Tourniquet applied above varices; the leg is milked upward.

Reproduced from the *Journal of the American Medical Association*.[14]

of the skin, or unusual or intractable ulceration of the leg is associated with varicose veins. Often this complication will be suggested by a history of milk leg or deep venous thrombosis. In any of these conditions, treatment of the primary condition should take precedence over operative treatment of the varicosities.

Since the tests for varicose veins serve only to identify and localize sites of valvular incompetency, a single simple test which is applicable to all or nearly all patients is desirable. A test which I believe fulfills these requirements and which can be used in place of the conventional procedures is the "retrograde leg-milking" test.[14]

Description of the Test

This test is performed with the patient standing on a low platform or chair. The patient's lower extremities are exposed to the groin. The examiner, who is seated facing the patient, first observes and palpates both saphenous systems and all varicosities and notes any skin changes in the legs. A tourniquet

FIGURE 5. After milking, the veins remain collapsed and then fill from below. There are no incompetent perforators present.

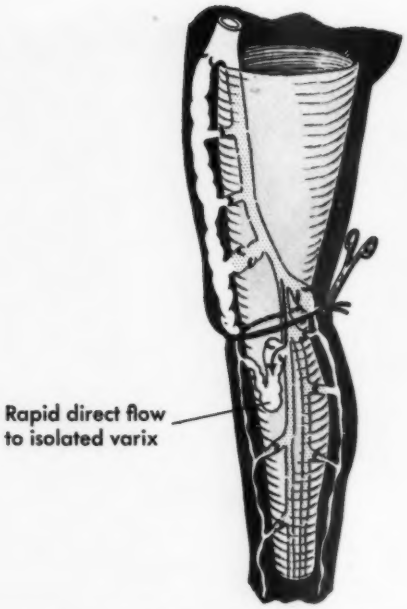


FIGURE 6. After milking, there is a reverse flow of blood into "blowout" from deep veins through an incompetent perforator.

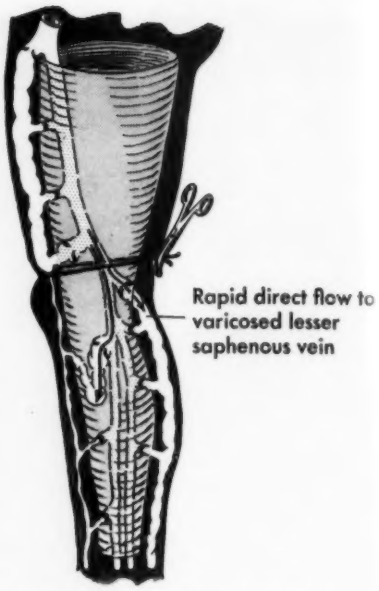
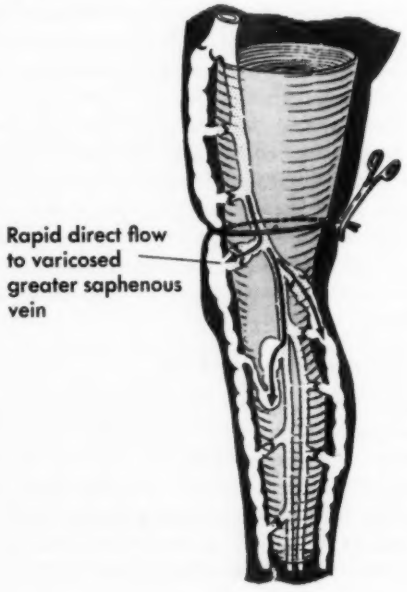


FIGURE 7. Tourniquet moved to a higher level. After milking, there is rapid filling of the lesser saphenous vein. There is incompetency of the valve at the saphenopopliteal junction.

FIGURE 8. Tourniquet moved to a higher level. After milking, there is rapid filling of the lower portion of the greater saphenous vein through a direct incompetent communicator.



(segment of rubber tubing) is then applied around the leg just above the lowest cluster of varicosities, just tightly enough to occlude the superficial but not the deep veins. The tourniquet should be fixed with a hemostat to prevent slippage. The skin is lubricated with water-soluble jelly (K-Y®); the examiner may wear rubber gloves if he so desires.

The milking maneuver is performed by the examiner, who encircles and compresses the tissues at the patient's ankle and rapidly moves his hands upward to the level of the tourniquet. The maneuver is repeated two or three times until all blood is milked from the superficial veins into the deep veins through communicating veins. When milking is complete it will be observed that the superficial veins are collapsed and that the skin is quite pale in comparison with the pink to cyanotic color of the opposite leg.

The examiner next studies the rate and manner in which the varicosity fills with blood. If it fills slowly (in about 30 seconds) from below, the implication is that there are no incom-

petent perforators below the level of the tourniquet (figures 3, 4 and 5). If, instead, there is rapid filling (in less than 10 seconds) confined to the varix, it is probable that an incompetent perforator exists in the region of the varix. Sometimes the presence of a perforator can be further substantiated by palpating a thrill and hearing a decrescendo murmur as the varix rapidly fills with blood. Palpation in this area also may reveal a hole in the deep fascia through which the communicating vein emerges to join the varix. Pressure at this point will delay filling of the varix.

When the rate and manner of filling of the varix are such that it is difficult to be sure if valvular incompetency does, in fact, exist, the examiner may ask the patient to strain (Valsalva's maneuver) in order to help answer the question. When peripheral venous pressure is increased and the valve is incompetent, blood will flow into the superficial veins rapidly, and the relative size of the shunt will be apparent.

After the area below the tourniquet has been studied, the tourniquet is moved to successively higher levels, depending on the distribution of the varicosities, and the same maneuvers and observations are repeated (figures 6, 7 and 8). Finally, the tourniquet is placed at the upper thigh, the entire leg is milked upward, and the function of the saphenofemoral valve is assessed. If this valve is incompetent, the varicosities will fill by reflux immediately after the tourniquet is released (figures 9 and 10).

By this means all possible points of valvular incompetency can be studied under direct vision. The patient can be turned or the lighting may be altered as required; the leg can be palpated or auscultated systematically; the milking can be repeated at any level; and, prior to operation, the sites of valvular incompetency may be marked with a suitable skin-marking solution.

During the examination, no changes in position are required and no unusual demands are made on the patient. Occasionally, tenderness or ulceration of the legs precludes application of this test. Rarely, the legs are so large that compression with the hands is impractical. Under these conditions the conventional tests

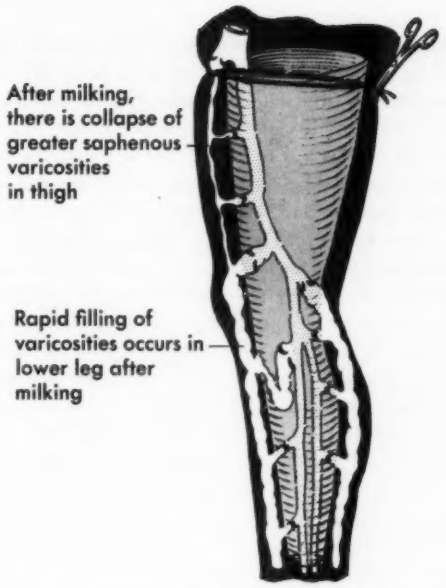
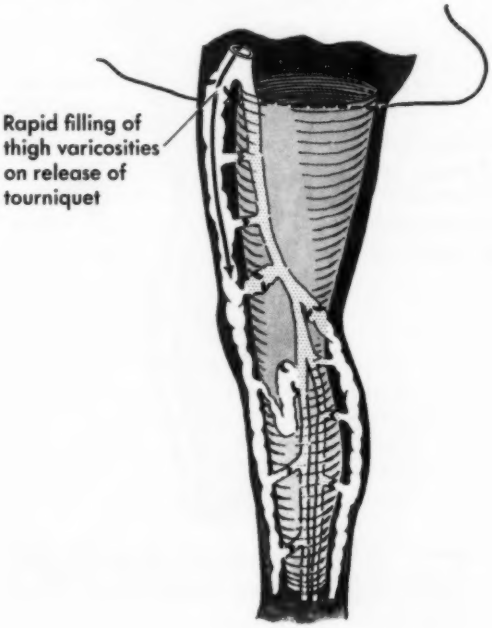

After milking, there is collapse of greater saphenous varicosities in thigh
Rapid filling of varicosities occurs in lower leg after milking

FIGURE 9. Tourniquet at groin level. After milking, the lower varicosities fill through the previously noted incompetent valves. The upper saphenous vein remains collapsed.

FIGURE 10. When the tourniquet at the groin is released, the upper thigh varicosities fill immediately. This indicates that the sapheno-femoral valve is incompetent.



should be used. Sometimes, when there are many scattered varicosities, it is advisable to use two or more tourniquets simultaneously. For example, during examination of the upper aspect of the leg or thigh, the second tourniquet is placed below the knee to prevent filling from incompetent perforators in the lower leg.

In patients with varicose veins secondary to extensive deep thrombosis, it is sometimes impossible to empty completely the varicosities by milking the leg (figure 11). This is because occlusion of the superficial veins with the tourniquet produces a marked rise in deep venous pressure. This finding suggests that the problem is not one of primary varicose veins, and that more extensive investigation is in order if any type of operative treatment is contemplated. As with any investigative procedure, the test is not a substitute for thinking; results must be interpreted according to the particular problem under study.

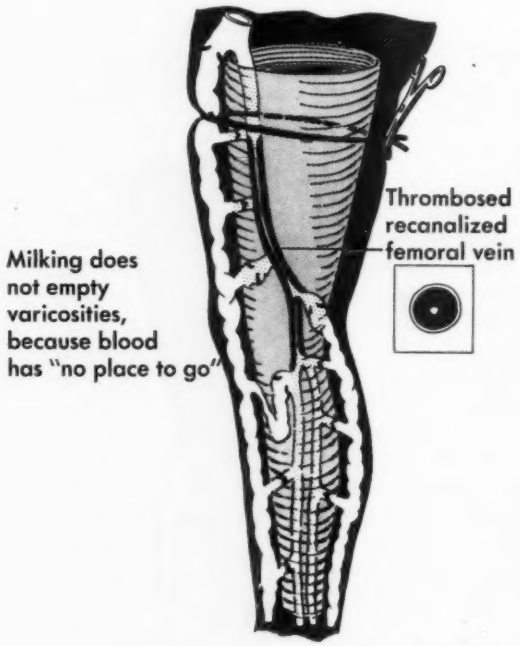


FIGURE 11. Extensive deep vein thrombosis with secondary varicosities. The varices may be difficult to empty by milking because of existing obstruction and valvular incompetency.

Discussion

The retrograde leg-milking test for varicose veins was first called to my attention about 10 years ago by Dr. J. A. Buckley of Portland, Oregon. It has since been used with success on innumerable patients and has been taught to many medical students and physicians. Although I have discussed tests for varicose veins with many surgeons, I have failed to find any who knew of the leg-milking test. A review of the literature also has failed to reveal a description of this test. It is likely, however, that this maneuver was previously described and then forgotten.

The retrograde leg-milking test actually combines many features of other tests used in the study of varicose veins. The veins of the legs are emptied by compression rather than by elevation, as in the Trendelenburg test. Compressing the leg from below and upward to the level of the tourniquet simulates the action of the leg-muscle pump, which is used to advantage in Perthes' test. However, in Perthes' test the leg must be moved as in walking, thus making inspection and palpation of varices very difficult or impossible. In the leg-milking test the patient does not have to move; however, in some cases the Valsalva maneuver may be used to bring out borderline or latent valvular insufficiency.

In patients treated largely by resident surgeons, the location of incompetent venous valves has been correlated with the findings at operation. The presence of perforators has been confirmed in approximately 84 per cent of instances. It is probable that with increased experience and attention to detail the correlation will be even higher.

Summary and Conclusions

1. Modern therapy of varicose veins involves ligation and stripping of all abnormally dilated veins and interruption of all sites of valvular insufficiency.

2. Prior to operation, detailed studies of the venous circulation should be carried out with respect to sites of valvular insufficiency.

3. The retrograde leg-milking test is a simple, easily applied maneuver which can be

used to identify and localize sites of valvular incompetency.

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Postgraduate Clinical NOTES

109. STUDY OF SYMPTOMS

The subjective complaint of his patient is, nearly always, the general practitioner's first point of contact with an individual whose well-being—or ill-being—becomes the doctor's privileged concern. In fact, this *is*, largely, the doctor-patient relationship, and it imposes on the doctor, first, the need to study symptoms and, second, the sanctity of the privilege. He must be a good listener, alert to the emphasis which the symptom expresses, so that he can classify, in his own way, the type of person he is dealing with. Broadly speaking, his patient, at the one extreme, is of the sympathetic type, or, at the other, the plethoric insensitive type; and the estimate of this psychosomatic balance is of the utmost importance in the privileged approach the doctor should adopt. The general practitioner who "treats 'em all alike" is, in spite of his honest John Bluntness, lamentably lacking in the very sensitivity to human variability which is essential in his own personal make-up. His estimate of the symptoms, in fact, depends to a large extent on his capacity for self-analysis, and the continued study of his patients' symptoms must be accompanied by a personal stocktaking at regular intervals. During this time of growth, he must be willing to admit, at least to himself, that he might be wrong, and what he was brought up to believe, both in morals and in medicine, might also be wrong, and that his adjustment to the dictates of authority is a requisite and natural result of his own development, ending, let us hope, in freedom of thought.

S. R. Wilson, For my son, now qualified, *Journal of Medical Education*, November 1958, pp. 797-808

From results obtained in a series of 399 esophagoscopic examinations, the authors determined the Eder-Hufford flexi-rigid esophagoscope to be superior to both the Boros and the Schindler instruments. They found that the flexi-rigid instrument eliminated the hazard of perforation, could be used even in the presence of acute hemorrhage, and was valuable in distinguishing disease of the esophagus from that of the stomach or duodenum. In several instances, the instrument was used at the patient's bedside.

Endoscopy With the Flexi-rigid Esophagoscope

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ESOPHAGOSCOPY has become a simpler and more readily available procedure since the introduction of the flexible-tipped esophagoscope,[1] and since its subsequent improvements and modifications.[2,3] The examination may now be performed in the office or, when necessary, at the bedside of the patient by physicians experienced with this diagnostic procedure.

Material

This report is based on a review of 339 consecutive esophagoscopic examinations performed with the flexi-rigid instrument at the Veterans Administration Hospital in West Haven, Connecticut, from June 1, 1953 to June 30, 1957, inclusive. These examinations were performed in a group of 219 cases. More than one examination was performed in 48 cases. In one case, the esophagoscopy was done 24 times in order to dilate an esophageal stricture. All of the patients had symptoms referable to the esophagus, such as dysphagia, pyrosis, vomiting and bleeding from the upper part of the gastrointestinal tract. In addition, the examination was performed in cases of portal hypertension in which the presence of esophageal varices was suspected.

In most of the cases, roentgenographic examination with barium was performed prior to esophagoscopy in order to rule out the possible presence of an obstructing lesion high in

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the esophagus. The only cases in which roentgenographic examination was not performed were those in which the patients recently had had gastrointestinal bleeding of undetermined origin. In such cases, early esophagoscopy is part of the aggressive diagnostic procedure.

Method of Examination

The patients were not permitted to eat breakfast on the morning of the examination. Approximately 60 minutes before the examination, 100 mg. of pentobarbital sodium was administered orally. A premedicant was administered hypodermically 15 minutes prior to the examination. This consisted of 0.4 to 0.6 mg. of atropine sulfate with either 10 mg. of morphine sulfate or 50 to 75 mg. of meperidine hydrochloride. Anesthesia of the pharynx was produced by the method of Selesnick.[4] For this purpose, we used 8 cc. of a 0.25 per cent solution of tetracaine hydrochloride, or a 1 per cent solution of BENADRYL® hydrochloride, or a 1 per cent solution of PYRIBENZAMINE® hydrochloride. Tetracaine hydrochloride was used for 228 examinations, Benadryl hydrochloride for 65, and Pyribenzamine hydrochloride for 45. No anesthesia was required for one examination.

The patient was placed in the left lateral decubitus position, as for gastroscopy, with his knees drawn up. An assistant held the patient's head fully flexed. The operator inserted the instrument by guiding it manually into the hypopharynx. When the tip of the instrument reached the proximal part of the esophagus, the patient was asked to swallow. When the cricopharyngeus muscle relaxed, the instrument was rapidly insinuated into the upper part of the esophagus. The patient's head was then extended, and the obturator of the instrument was withdrawn. The rest of the examination was conducted under direct vision. The instrument was passed into the stomach whenever possible.

During withdrawal of the instrument, the entire circumference of the esophagus was scrutinized at all levels. If indicated, biopsy specimens of the esophageal mucosa or of any visible lesions were taken with esophageal biopsy forceps.

Initially, the Boros,[1] the Schindler,[3] and the Eder-Hufford[2] instruments were used alternately, but subsequently all examinations were performed with the Eder-Hufford flexi-rigid esophagoscope. The Boros instrument was used for 26 examinations, the Schindler instrument for 96, and the Eder-Hufford instrument for 217.

After completion of the examination, the patient was returned to the ward, and was permitted to eat two hours later. Outpatients remained in the hospital only long enough for the effects of the medication to subside, which usually was about two hours.

TABLE 1

CAUSES OF 17 INCOMPLETE EXAMINATIONS

CAUSES	NUMBER
Failure to pass the incisors	5
Cricopharyngeal spasm	1
Panic of patient	4
Inability to insert instrument into thoracic stomach	2
Anterior angulation at 30 cm.	3
Not recorded	2
TOTAL	17

TABLE 2

POSITIVE RESULTS OF 199 EXAMINATIONS

RESULTS	EXAMINATIONS
Esophagitis	56
Stricture	30
Esophageal varices	27
Carcinoma	20
Hiatus hernia	20
Esophagitis and stricture	14
Cardiospasm	8
Esophagogastrostomy	5
Diverticulum	3
Redundant folds	3
Leukoplakia	2
Benign submucosal lesion	2
Hereditary familial telangiectasia	1
Papilloma	1
Schatzki ring	1
Scleroderma	1
Chalasia	1
Motor dyskinesia	1
Esophagojejunostomy	1
Radiation esophagitis	1
Gastritis	1
TOTAL	199

Results

One hundred and twenty-three of the examinations did not reveal any abnormality. Seventeen of the examinations could not be completed. The causes of the failure to complete these examinations are listed in table 1. In the four instances in which panic on the part of the patients necessitated withdrawal of the instrument, the examination subsequently was performed without difficulty after the patients had been reassured. There were positive findings in 199 of the examinations (table 2). No morbidity or mortality resulted from the examination, and none of the patients refused to undergo a second examination when they were requested to do so.

Comment

The advantage of the Schindler esophagoscope over the original Boros instrument is that the rigid tube, which contains the obturator with a short rubber tip on its end, can be passed immediately after it is introduced. As soon as the instrument enters the esophagus, the obturator is withdrawn, and the optical system is inserted. The Eder-Hufford instrument has two important modifications: (1) It has an adjustable obturator with a long rubber tip, which enables its length to be varied according to the patient and the site of the lesion, and (2) it contains a simple optical system, which avoids manipulation of the instrument after the obturator is withdrawn.

A major hazard of esophagoscopy performed with the standard rigid instrument is perforation of the esophagus or hypopharynx. Seybold, Johnson and Leary[5] reported the occurrence of perforation in 19 cases. In 17 cases, the perforation occurred in the cervical portion of the esophagus. Palmer[6] said that most perforations due to endoscopy occur just proximal to the cricopharyngeus muscle. Several factors are responsible for the occurrence of perforation at this site. The cricopharyngeus muscle is contracted at rest and relaxes only during deglutition. If the patient cannot swallow, the instrument must be pushed against a contracted muscle, and injury of the mucosa is possible. If a general anesthetic is used, the patient cannot cooperate with the operator, and this increases the risk of perforation. The relative sparcity of posterior musculature in the distal portion of the hypopharynx increases the hazard. The cervical portion of the spinal column with its bony prominences is pressed against the esophagus. This is particularly dangerous in elderly patients who have hypertrophic cervical arthritis. When the patient's head is fully extended during introduction of the rigid esophagoscope, the effect of the cervical segment of the vertebral column compressing the esophageal wall against the instrument is increased.

No morbidity or mortality resulted from the 339 examinations reported in this paper. By using the flexi-rigid esophagoscope, endoscopy was performed without hazard, even in the presence of acute hemorrhage from the upper part of the gastrointestinal tract. It proved to be of definite value in distinguishing disease of the esophagus from disease of the stomach or duodenum.[7] In several cases, the examination was done while the patients were in bed.

Because of the simple preparation needed, examination with the flexi-rigid esophagoscope can be performed readily in the office or as a clinical procedure. Our practice is to have the patient come to the office for premedication two or three hours before the examination is scheduled. It is desirable to observe the patient for two hours after the examination.

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Infection causes many stillbirths and neonatal deaths. It may be acquired prenatally from the mother or postnatally in the nursery. If the possibility of intrauterine infection exists, the author recommends that the infant should be treated from the moment of birth. Prophylactic therapy has been found useful in nursery epidemics caused by staphylococcal organisms. Use of human blood products in overcoming deficiencies in infants' defense mechanisms is being investigated.

Infection as a Cause of Death in the Perinatal Period

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In most medical centers, the total number of stillbirths and neonatal deaths, now commonly called perinatal mortality, varies from 24 to 32 per 1000 births. These figures indicate a perinatal mortality of about 100 in the 4000 deliveries per year at the Maternity Pavilion of the Winnipeg General Hospital. Of this number, approximately 50 are stillbirths.[1,2]

The need for a concentrated attack to lower this mortality is evident. In planning such an attack, one scans the available data on causes of perinatal death, seeking ways to develop methods to prevent some of the deaths.

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Common Causes of Perinatal Death

Although this presentation is primarily a review of the solved and unsolved problems relating to infection as a cause of perinatal death, other common causes also should be mentioned. Postmortem findings show that, in addition to infection, trauma, hemolytic disease, anoxia, congenital malformations and abnormal pulmonary ventilation syndromes are the chief primary causes of death in the perinatal period (table 1).

Trauma—Deaths due to trauma often may be prevented. Further improvement in obstetric technics and insistence on high professional standards already have effected notable improvement in this area, and they will continue to do so.

Hemolytic disease—If present-day knowledge of hemolytic disease of the newborn is made available to all who care for infants with this condition, perinatal deaths associated with this disease will be reduced. A high standard of technical competence and an or-

TABLE 1

PERCENTAGES OF INFANT DEATHS DUE TO ANATOMIC CAUSES*

POSTMORTEM FINDINGS†	CHICAGO AREA	NEW YORK AREA	LONDON HOSPITAL	WINNIPEG HOSPITAL
Abnormal pulmonary ventilation and diffusion	47.5	40.0	26.6	27.7
Malformations	13.5	19.0	15.0	14.4
Anoxia	4.2	5.0	5.0	13.8
Infection	10.0	5.0	12.2	12.6
Hemolytic disease of newborn	—	10.5	3.2	6.6
Trauma	18.3	17.0	18.1	6.0
Miscellaneous	1.0	—	5.4	5.4
Inconclusive or unknown	—	4.0	—	7.8

*The percentages of prematures in these studies were 79.1, 54.2, 71.8 and 68.0, respectively; total deaths in each study were 10,000, 955, 221 and 160.

†The percentages of autopsies performed in each study were 89.0, 35.0, 100.0 and 92.0, respectively.

ganization geared to anticipate and prepared to treat this condition are essential.

Anoxia—Many stillbirths and deaths within the first few minutes or hour of life are caused by anoxia. Improvement in combating this condition depends on earlier recognition of fetal distress and a better understanding of the mechanisms that are involved in toxemia of pregnancy.

Congenital malformations—Remediable congenital malformations are now recognized with more certainty, and surgical treatment of such conditions has saved many newborns. Future emphasis will be on preventing malformations by controlling at least some of the factors responsible for embryonic injury.

Abnormal pulmonary ventilation—Deaths associated with abnormal pulmonary ventilation will continue to account for one-fourth of the perinatal mortality until we learn how to reduce the incidence of prematurity and how to treat the respiratory distress syndrome which so often accompanies it.

Recognition of Infection

Although infection causes approximately 12 per cent of all perinatal deaths, its importance is often overlooked, especially in medical centers in which few autopsies are performed. Table 1 shows that in places where autopsy rates are low the mortality attributed to infection is also low. This simply means that infection often is not diagnosed while the infant is living. Our records contain several examples of sick infants who were treated for presumed intracranial or cardiac disease but who were found at autopsy to have sepsis, with no evidence of pathologic abnormalities in the brain or heart. It also means that some stillbirths which occur without evident clinical explanation may be shown at autopsy to be the result of intra-uterine infection. We have encountered several such instances. If autopsies had not been performed, the real reasons for the stillbirths might never have been known.

Obviously, infection in the nursery infant may be difficult for even the most experienced observer to recognize. Fever and the usual signs of respiratory sepsis may not be present. There may be listlessness, inability or unwillingness to nurse, vague periods of tachypnea or apnea, occasional cyanotic spells, convulsions, subnormal or normal temperature, and, of course, poor weight gain. Twitching and convulsions may simulate trouble in the central nervous system. Cyanotic spells may suggest congenital heart disease. Jaundice and a raised leukocyte count may imitate hemolytic disease or blood dyscrasia.

Prenatal Infection

How can we achieve better management of prenatally acquired infection and thereby raise the survival rate of infected babies? Three possible approaches to this problem are listed in table 2.

TABLE 2

MANAGEMENT OF PRENATALLY ACQUIRED INFECTION

1. Treatment of infant from the moment of birth when possibility of intra-uterine infection exists.
2. Earlier recognition of possibility of prenatal infection of baby and prophylactic treatment of mother with antibiotics appropriate for the organisms commonly involved.
3. Efforts to overcome possible defects in the newborn's mechanisms of defense against infection.

Postnatal Infection

The organisms implicated in postnatally acquired infection are indicated in table 3. Although these infections are more likely to occur in outbreaks, they may affect an isolated infant. The hospital nursery can be a dangerous place for the infant unless strict precautions are maintained to prevent entry and spread of infection. Rules outlining the proper procedures to follow in nurseries have been published by the American Academy of Pediatrics[3] and should be strictly enforced.

A great deal of infection in the nurseries of most hospitals is attributable to staphylococcal organisms. This group of infections does not contribute materially to mortality in the nursery period, but it is responsible for initiating shared family staphylococcal disease which may culminate in the development of generalized sepsis, pneumonia or serious localized pyogenic lesions in the newborn. Eternal vigilance in the nursery is essential if outbreaks of epidemic staphylococcal disease are to be prevented.

We have had more than one encounter with this problem. An outbreak of skin pustules in nursery infants and breast abscess in their mothers occurred in 1949. As many as 80 per cent of the infants were affected; at one point breast abscess developed in 20 per cent of the mothers within a month after they left the maternity ward. The organism responsible was a coagulase-positive *Staphylococcus* which was sensitive to AUREOMYCIN® and resistant to penicillin. It was found in the nose cultures of nursery infants within 24 hours of birth. Efforts to find a carrier among hospital personnel, physicians and visitors to patients proved fruitless.

Instituting rigid precautionary technic made little impression on the outbreak. The prophylactic use of Aureomycin, which had just become commercially available, quickly ended the epidemic. This method of prophylaxis was used first in all infants in one of the two nursery wards involved; the other ward served as a control. Within a week it was evident that this treatment was the immediate answer to the emergency. Controls were discontinued and the prophylactic treatment was employed for many weeks.

In 1956 we determined that a small outbreak of pyoderma in our nurseries was caused by a bacteriophage-positive *Staphylococcus*, sensitive only to CHLOROMYCETIN®. In this instance a carrier (a ward aid) was found among the hospital personnel. After she had been dismissed from the nursery, the outbreak was quickly controlled.

Routine administration of an appropriate prophylactic agent to the entire nursery population to cope with a sudden epidemic of staphylococcal disease in a nursery has been reported by others. Erythromycin was used by Shaffer;[4] Langewisch[5] used penicillin to control an epidemic of streptococcal infection. Except in emergencies, extensive and indiscriminate prophylaxis of nursery infants should not be encouraged. More important is the immediate recognition and isolation of the source of the outbreak. Many investigators

TABLE 3

ETIOLOGY OF INFECTION IN THE NURSERY INFANT

Infection acquired postnatally
1. Bacterial (*Staphylococcus, Streptococcus, Escherichia coli, Hemophilus influenzae, Pseudomonas aeruginosa*)
2. Viral
3. Mycotic (*Candida albicans*)

Infection acquired prenatally
1. Blood-borne (shared bacterial or viral infection)
2. Ascending infection via birth canal (*Esch. coli, Ps. aeruginosa*)
   a. With premature rupture of membranes
   b. With intact membranes
3. Contact infection (thrush, gonorrheal ophthalmia)

have found carriers among nursery personnel. In these instances, the outbreak has been controlled after the carrier has no longer entered the nursery.

It is not difficult to recognize infection in a nursery infant when the skin, umbilicus or mouth is involved. In many instances, however, the clinical picture may be difficult to assess. It becomes necessary to assume that infection is present in any nursery infant who, after a day or two of apparently normal progress, becomes listless, refuses to eat, or shows any of the previously mentioned signs and symptoms without evident clinical findings. As soon as preliminary steps are taken to identify the infection, empirical treatment should be started with penicillin, streptomycin and chloramphenicol or oxytetracycline. Some infants will be treated unnecessarily, but some will survive who otherwise may have died. Blood, urine and umbilical stump cultures, chest x-ray and, occasionally, spinal puncture are necessary steps in the process of identifying the causative agent.

Clinical Features of Infection

Some of the peculiarities which characterize infection in the nursery infant are listed in table 4. Infection may be acquired before birth from the mother either as a shared bacterial, viral or parasitic infection or as a result of infected membranes in the maternal birth passage. Often, the organisms concerned are enteric bacteria, harmless to the mother but exceedingly dangerous for the infant.

Nursery epidemics still occur from time to time. It is well known that the newborn, particularly the premature, has a lowered resistance to disease. The factors involved are only now beginning to come to light. Peculiarities and deficiencies in the defense mechanisms of the nursery infant result in a tendency for infection to become generalized. The urinary tract and central nervous system are particularly prone to involvement.

The difficulties of recognizing infection in the nursery infant have been mentioned previously. If lives are to be saved, it is important for the physician to anticipate infection and to realize the necessity of starting investigation and instituting treatment on an empirical basis without waiting for laboratory and radiologic proof of infection.

TABLE 4

PECULIARITIES OF INFECTION IN THE NURSERY INFANT

1. Infection may be acquired prenatally from mother or postnatally in nursery from other infants or infected carriers.
2. The umbilical stump, skin or mucous membranes may be the site of entrance. Ingested or aspirated infected amniotic fluid may lead to sepsis.
3. Infection tends to be generalized; the urinary tract and central nervous system often are involved.
4. Organisms nonpathogenic for older age groups (*Esch. coli, Str. faecalis, Ps. aeruginosa*) may cause severe sepsis.
5. Infants' defense mechanisms may be inadequate.
   a. Humoral—lack of specific antibody; (?) deficiency of properdin.
   b. Cellular—defective phagocytosis.
6. Clinical picture may be deceptive.

Treatment

Treatment of infant—In cases in which the possibility of infection exists, we have not been very successful in using routine prophylaxis in infants from the moment of birth. We have used a combination of 20,000 units crystalline penicillin every four hours; 50 mg. chloramphenicol per kilogram of body weight per day, divided into four doses; and 75 mg. streptomycin per kilogram of body weight per day, divided into two doses. Of course, it is possible that we may have prevented generalized sepsis in some cases. However, autopsies have demonstrated that infection has developed in some infants in spite of the routine prophylaxis. The following case report from our files is an example of such a failure.

The infant's expected birth date was June 14, 1957. The mother's membranes ruptured April 16, 1957, and the baby was born April 21, 1957. The birth weight was 2,670 gm. The baby's respirations at birth were labored. Because of premature rupture of membranes, the routine administration of antibiotics (penicillin, streptomycin and chloramphenicol) was started at birth. There was x-ray evidence of pneumonitis. Treatment continued until the baby died on April 25, 1957. An au-

topsy showed that the infant had had bilateral pneumonia. The placenta showed evidence of acute amnionitis and vasculitis.

There are objections to routine antibiotic prophylaxis, whether it is used for the mother or the infant. The undesirable consequences of such a routine in a hospital are self-evident, but carefully controlled studies are necessary to show whether the advantages outweigh the disadvantages. Routine prophylaxis seems reasonable if the following conditions are present:

1. Membranes ruptured for longer than 18 hours.
2. Evidence of maternal fever at delivery.
3. Murky amniotic fluid.
4. Prolonged difficult labor.
5. Obstetric or resuscitative procedure involving instrumentation.

If prophylactic treatment is to have any degree of success it must be started at the moment of birth. Some infants will receive treatment unnecessarily, but if this procedure results in saving some lives it would seem justified.

Treatment of mother—The maternal role in the problem of infection is important. We can hardly hope to alter the result in babies who die within 24 hours of birth from infection they acquire from their mothers unless the obstetrician is better able to anticipate prenatal infection and to initiate preventive treatment. Perhaps there has been too much concentration on the problems of sterilizing the amniotic fluid and too little on ridding the genital tract of organisms which, although harmless to the mother, can cause death in the infant. The organisms with which we are concerned are *Esch. coli, Str. faecalis,* nonhemolytic *Streptococcus* and *Staph. aureus.*

In this regard, the work of McCredie Smith, Jennison and Langlay[6] is significant even if it is not statistically perfect. They suggested that it is possible to predict the occurrence of perinatal infection, and that if given a 48 hour period one may reduce the genital bacteriologic flora and decrease the risk to the baby. We are now pursuing this study in cooperation with the departments of obstetrics and bacteriology. It seems important to reconsider the prevailing theory that maternal prophylaxis instituted before labor actually begins is valueless. We must remember that this view was based on the use of penicillin alone, and that the organisms with which we are concerned ordinarily are not affected by this drug.

The Infant's Defense Mechanisms

What are the defense mechanisms of the infant, especially of the premature, who figures so largely in our statistics of death due to infection? A hopeful beginning to the solution of the problems involved has been initiated by the work of Gluck and Silverman,[7] who drew attention to defective phagocytosis in prematures, and of Pillemer and co-workers,[8] who studied the action of properdin.

These two investigations, along with the work of several others in this field, reveal a great gap in our knowledge of the various factors which enable us to resist infection. It seems clear that the newborn, especially the premature, may be deficient in both cellular and humoral elements which may determine success or failure in the body's reaction to an infectious agent.

The possibility of administering carefully prepared blood products which may overcome some of these deficiencies in the newborn is already being investigated. It has been shown experimentally that adult serum will improve the efficiency of phagocytosis of the premature's cells, and that normal adult serum can supply specific antibodies as well as nonspecific substances such as properdin. This calls to mind the good results that often followed the empirical administration of whole blood to sick newborns a quarter of a century ago. Use of this procedure declined rapidly in popularity as empiricism came into disfavor when its possible dangers were realized. As we gain more knowledge of the preparation of blood products and their fractions, it is quite possible that we may return to the use of these substances to help premature and newborn infants who have defective defense mechanisms survive prenatally acquired infection.

Summary

1. The common causes of death in the perinatal period are reviewed.

2. The importance of infection as a cause of stillbirth or death in the nursery period is stressed.

3. Methods of preventing perinatal deaths due to infection are discussed, with particular reference to the importance of early recognition and prophylaxis of potential prenatal intra-uterine infection.

4. Defects in neonatal mechanisms designed to combat infection are mentioned, and the possible role of human blood products in overcoming these defects is discussed.

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Books Received

Books received are acknowledged, and, as space permits, those of principal interest to our readers are reviewed more extensively. Reviews appear in this issue starting on page A-154; additional listings are on pages 294 and A-164.

The Year Book of Drug Therapy (1958-1959). Edited by Harry Beckman, M.D., Director, Departments of Pharmacology, Marquette University Schools of Medicine and Dentistry, Milwaukee. 569 pages with 43 illustrations. 1959, The Year Book Publishers, Inc., Chicago. $7.50.

The Pneumoconiosis Problem; With Emphasis on the Role of the Radiologist. By Eugene P. Pendergrass, M.D., Professor of Radiology, University of Pennsylvania School of Medicine, Philadelphia. 146 pages with 53 illustrations. 1959, Charles C Thomas, Springfield, Illinois. $6.75.

The Chemical Prevention of Cardiac Necroses. By Hans Selye, M.D., Professor and Director, Institute of Experimental Medicine and Surgery, University of Montreal, Montreal, Canada. 235 pages with 20 illustrations. 1958, The Ronald Press Company, New York. $7.50.

Handbook of Cardiology for Nurses. By Walter Modell, M.D., Associate Professor, Cornell University Medical College, and Doris R. Schwartz, B.S., Assistant Professor, Cornell University-New York Hospital School of Nursing, New York. Ed. 3. 328 pages. 1958, Springer Publishing Company, Inc., New York. $4.50.

Growth and Development of Children. By Ernest H. Watson, M.D., Professor, and George H. Lowrey, M.D., Associate Professor, Department of Pediatrics and Communicable Diseases, University of Michigan Medical School, Ann Arbor. Ed. 3. 334 pages with 74 illustrations. 1958, The Year Book Publishers, Inc., Chicago. $7.75.

Diagnostic Bacteriology. By Isabelle G. Schaub, A.B., Assistant Professor of Microbiology, The Johns Hopkins University School of Medicine, M. Kathleen Foley, M.A., Assistant Professor of Biological Sciences, College of Notre Dame of Maryland, Baltimore, Elvyn G. Scott, M.T., Bacteriologist-in-Charge, Department of Bacteriology, The Delaware Hospital, Wilmington, and W. Robert Bailey, Ph.D., Associate Professor of Biological Sciences, University of Delaware, Newark. Ed. 5. 338 pages, illustrated. 1958, The C. V. Mosby Company, St. Louis. $4.75.

British Medical Bulletin. Haematology. Symposium, prepared by 17 contributors. Vol. 15. No. 1. 88 pages. 1959, Medical Department, The British Council, London. $3.25.

Treatment in Internal Medicine. By Harold Thomas Hyman, M.D., Formerly, Assistant Professor of Pharmacology, Columbia University College of Physicians and Surgeons, New York. 609 pages. 1958, J. B. Lippincott Company, Philadelphia and Montreal. $12.50.

Around the Clock Aids for the Child With Muscular Dystrophy. By Morton Edwards. 32 pages, illustrated. 1959, published and distributed by The Muscular Dystrophy Association of America, 1790 Broadway, New York 19. $0.25.

Atlas of Technics in Surgery. By John L. Madden, M.D., Director of Surgery, St. Clare's Hospital, New York, with 62 contributors. 648 pages with 293 plates. 1958, Appleton-Century-Crofts, Inc., New York. $30.00.

The Demonstration Clinic. For the psychologic study and treatment of mother and child in medical practice. By David M. Levy, M.D., Clinical Professor of Psychiatry, Columbia University College of Physicians and Surgeons, New York. 120 pages. 1959, Charles C Thomas, Springfield, Illinois. $5.00.

Two unique cases are presented to illustrate that combinations of dislocations among carpal bones are practically limitless. The authors describe a perilunar dislocation in a diabetic patient which was reduced under general anesthesia. However, because the carpal navicular could not be stabilized, arthrodesis of the wrist was carried out. They also review a manipulative reduction performed for dislocation of the distal portion of the radio-ulnar joint with anterior displacement of the distal portion of the ulna.

Two Unusual Wrist Injuries

JOHN A. HARTWIG* AND EINER W. JOHNSON, JR.†

Mayo Clinic and Mayo Foundation, Rochester, Minnesota

A FALL or severe force on the outstretched hand accounts for a great number of fractures and dislocations seen by the physician in a practice where the injuries of ordinary day-to-day trauma are seen and treated. This form of trauma results in a variety of injuries to the upper extremity. The type of injury, of course, varies with the age of the patient. In children the common injuries produced by this form of trauma are epiphysial separation of the distal radial epiphysis, fracture of the forearm, or fracture or dislocation of the head of the radius. In adolescents and young adults fracture of the carpal navicular probably occurs most commonly as a result of a fall on the outstretched hand, while in elderly persons Colles' fracture is the most often produced injury.

Other injuries produced by this mechanism but less frequently seen are dislocations of the semilunar bone, perilunar dislocations of the carpus, separations of the distal radio-ulnar joint with fracture of the radial head (the so-called Essex-Lopresti fracture-dislocation), dislocation of the elbow, fractures of the humerus, dislocations of the shoulders, and fractures of the acromion.

JOHN A. HARTWIG

EINER W. JOHNSON, JR.

The following two cases are presented because of the unusual wrist injuries; injury in one case resulted from a fall on the outstretched hand, and in the other it occurred in an automobile accident where the injuring force was probably quite similar. The first case presented a somewhat unusual problem in treatment.

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FIGURE 1. Anteroposterior view showing perilunar dislocation of the left carpus with fracture of the radial styloid.

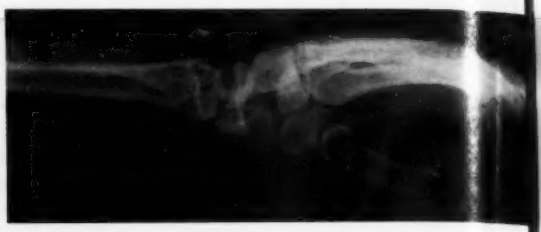

FIGURE 2. Lateral view of the left wrist showing perilunar dislocation. Note that the navicular has lost its normal relationship to the radius.

Case Reports

Case 1—A 54 year old diabetic hypertensive housewife was involved in an automobile accident on March 1, 1957. She was seated in the rear seat on the right side when the car in which she was riding slid into a ditch. She received multiple contusions and abrasions of the face, right elbow, left hand and wrist, and left pretibial area. She was admitted to a small local hospital where first-aid treatment was given and the presence of glycosuria was discovered. Because of the discovery of glycosuria she was transferred to St. Marys Hospital, Rochester, Minnesota, the following day, 24 hours after the injury, her left wrist having been placed in a splint.

On examination her pulse rate was found to be 86 beats per minute; the blood pressure was 160 mm. of mercury systolic and 100 mm. diastolic, and the oral temperature was 98.6° F. The essential physical findings were extensive facial ecchymoses and moderate swelling of the left wrist without deformity.

Roentgenograms revealed a perilunar dislocation of the left wrist with fracture of the styloid process of the radius (figure 1). Two days later, on March 4, 1957, after her diabetes had been assessed and diabetic treatment instituted, a closed reduction of the wrist was attempted with the patient under general anesthesia.

The perilunar dislocation was essentially reduced by the foregoing procedure, but the carpal navicular remained dislocated and

FIGURE 3. Anteroposterior view of the left wrist after closed manipulation. Note that the perilunar dislocation has been reduced, but reduction of the navicular has been prevented by interposition of the fractured fragment from the radial styloid.

FIGURE 4a. Anteroposterior view of left wrist four and a half months after arthrodesis showing reduction of the navicular and tibial graft in place extending from the radius to the third metacarpal. b. Lateral view of left wrist showing tibial graft in place spanning the carpus (case 1).

could not be reduced (figure 2). The fragment from the radial styloid prevented reduction of the navicular (figure 3). Open exploration of the wrist was advised and was discussed with the patient. She stated the desire to have only one operation and requested that the operation be done which would give her the best functional result and still make it unnecessary for any further surgical procedures. For this reason arthrodesis of the wrist was discussed with her.

Twelve days after injury, the wrist was explored through a dorsal longitudinal incision. The loose fragment of the styloid process of the radius was excised. It was then possible to reduce the dislocated navicular bone but the reduction was extremely unstable. Therefore Brittain arthrodesis of the left wrist was done with bone for the graft taken from the patient's tibia.

The patient's convalescence was uneventful. At the time of last examination four and one-half months after operation her wrist was painless, function of the hand was normal, and, aside from the surgical scar, the wrist was cosmetically indistinguishable from the opposite wrist (figure 4a and b).

Case 2—An 87 year old woman stumbled and fell in her bedroom in the dark, landing on her outstretched hand and injuring her left wrist. Because of swelling and deformity she was brought to the emergency room at St. Marys Hospital two days later on March 2, 1957. She also complained of some pain in the midportion of her back when active, but the pain was readily relieved by rest.

Her history was not remarkable except for urinary frequency, urgency and occasional incontinence. No definite history of polyuria could be obtained.

On examination her pulse was 90 beats per minute; her blood pressure was 178 mm. of mercury systolic and 90 mm. diastolic, and her oral temperature was 98.6° F. Cardiac size was normal with a normal sinus rhythm and a diffuse systolic murmur, grade 1, heard best at the apex. Minimal basilar rales were heard over both lungs. There was prominence of the distal ulna on its volar aspect with moderate swelling, and the distal forearm seemed

FIGURE 5. Anteroposterior view of left wrist showing dislocation of the distal radio-ulnar joint. Note the soft tissue swelling and loss of normal conformity of the wrist.

narrowed when compared with the opposite member. There was no evidence of neurologic deficiency.

Urinalysis revealed glycosuria, grade 2; fasting blood sugar measured 115 mg. per 100 cc.

A roentgenogram of the left wrist revealed evidence of a dislocation of the distal radio-ulnar joint with anterior displacement of the distal portion of the ulna with the result that it presented on the volar aspect of the distal radius (figure 5).

On the day of admission, which was 48 hours after injury, local anesthesia was given and closed manipulative reduction was performed. Dorsal and ventral plaster splints were applied. The procedure was well toler-

FIGURE 6. Anteroposterior view of left wrist after reduction and restoration of the normal relationship between the distal part of the radius and that of the ulna.

ated, and the cosmetic appearance of the extremity was restored (figure 6).

The patient was kept in the hospital because it was discovered that she had diabetes. On March 4, 1957, auricular fibrillation with evidence of early cardiac failure developed and she was digitalized. She finally complained of thoracic pain, and dyspnea developed. The presumptive diagnosis of myocardial infarction was made, and she was placed on a coronary regimen. She deteriorated rapidly and died on March 8, 1957, six days after admission. Necropsy revealed old and recent myocardial infarcts.

Comment

These two cases illustrate the fact that there is practically no limit to the number of combinations of dislocations among the carpal bones. Frequently exact roentgenographic interpretation of the injury is difficult, and when in doubt a roentgenogram of the opposite wrist should be made for comparison. Also of value in determining the presence or absence of carpal dislocation is the fact that in the anteroposterior view of the wrist all carpal bones except the pisiform can be seen in their entirety without undue overlap of one margin on that of its neighbor. Certainly, too, adequate interrogation of the patient about the method of injury and thorough inspection and palpation of the wrist are helpful in arriving at a correct diagnosis. Neurologic changes occasioned by pressure on the median nerve at the ulnar styloid should be watched for; when present they constitute one reason for reduction at the earliest possible time.

In case 1 the perilunar dislocation was rather easily reduced by closed means. However, the navicular could never be firmly seated in the curve of the distal part of the radius because of the interposition of the loose fragment from the radial styloid. Even when this fragment was removed at the time of operation and the navicular restored to its proper place, the navicular was markedly unstable. Because of this instability occasioned by rupture of its ligaments, and because of the imminence of aseptic necrosis of the navicular, arthrodesis of the wrist was carried out.

Case 2 is presented solely because the injury was unique.

Postgraduate Clinical NOTES

110. NEURITIS

In general, but only in general, it may be said that when neuritis affects one nerve (mononeuritis), adjacent nerves, or a plexus of nerves, the cause commonly is a mechanical one; that when several, single major nerves are affected simultaneously, a situation that may be described as mononeuritis multiplex, the cause is often a vascular or allergic one; and that when nerves are affected diffusely, as in the disorder known as multiple neuritis, the cause is often a toxic, viral, metabolic or allergic one, rarely an hereditary one. Finally, it is well to note that various causes of neuritis, as is true of so many debts, are cumulative.

Henry W. Woltman and Norman P. Goldstein, Some where's and why's of neuritis, *Neurology*, March 1958, pp. 187-192

Sufficiently large amounts of ionizing radiation can cause death; possible nonlethal effects of large doses include cancer, atrophy of irradiated tissue, depression of immune reactions, and sterility. The authors claim that x-ray examination is justified only when diagnostic benefits outweigh the hazards. Results of a study to determine the amount of gonadal and bodily exposure during common x-ray examinations at a typical hospital are presented along with measures to be taken to reduce the gonadal dose.

Hazards and Precautions for the Patient and the Doctor in Diagnostic Roentgenology

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ALTHOUGH x-rays and other ionizing radiations play a vital role in modern medicine, they are unfortunately capable of harming both the doctor and his patients. Ionizing radiation in sufficiently large amounts can produce death; smaller, but still large, doses cause many different changes in the body and in its cells, nearly all harmful. Some of the nonlethal effects of large doses include cancer, atrophy of irradiated tissue, manifesting itself, e.g., as chronic dermatitis, hemorrhage and anemia, depression of immune reactions, and sterility. At the cellular level, inactivation of enzymes and denaturation of protein can result with large doses. The interferences with vital cell functions caused by even the lowest doses are the important effects which must be considered by the physician employing x-rays in diagnosis. A single hit may produce a gene mutation, and any cell may be killed genetically (i.e., prevented ever from dividing again) by two critical hits provided they occur within a short time.[1]

Because it takes only one hit in the vicinity of a gene, any dose of radiation, no matter how small, will result in mutations in either germ cells or somatic cells. Whether these mutations occur in germ cells or somatic cells makes some difference. Mutations in the germ cells produce hereditary defects. Mutations in somatic body cells may be one of the causative agents of all kinds of cancer, including leukemia; somatic mutations may also be involved in the phenomenon of aging.[2]

An inherited genetic defect can cause outright death of the offspring, or the radiation-induced change in a gene may be transmitted for several generations before it becomes evident. The overwhelming majority of mutant

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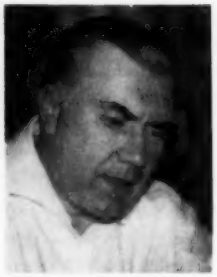

DIMITRY MORKOVIN

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genes lead to some kind of harmful effect. Some may cause small handicaps which tend to increase susceptibility to disease and result in shortened life, or they may result in partial or complete sterility. Others may produce severe anomalies. Among the major congenital anomalies resulting from mutations, still consistent with life, in dominant genes are: achondroplasia, epiloia, retinoblastoma, change in hair pigment, eye and hearing defects (Waardenburg's syndrome), multiple polyposis of the colon, dystrophia myotonica, Marfan's syndrome and aniridia. Mutations in sex-linked recessive genes give rise to diseases such as hemophilia and Duchenne's type of muscular dystrophy.

Mutated genes consistent with life are often recessive. If a child gets a mutated gene from one parent and a normal gene from the other parent, the normal gene may be able to assure normal function except at times when the demand for the function governed by that particular gene is heavy. Therefore, the large majority of mutations will not be detectable in the first generation of offspring of the person who received the radiation. However, if both mother and father have the same mutated gene, the offspring may manifest a detectable anomaly.

Since large numbers of the population are being exposed to increasing amounts of mutagenic materials and energy, it is imperative that persons who are responsible for the exposure and those who are being exposed should try to reduce their share of the hazards.

The Medical Research Council of Great Britain[3] has reported that 10 to 20 per cent of spontaneously occurring mutations are attributable to background radiation. According to a report[4] by the National Academy of Sciences, the 30 year gonadal dose received by the average person in the United States is 4.3 r from background radiation, that is, from cosmic rays and naturally occurring radioisotopes, and 3 r from roentgenographic and fluoroscopic examination.

Results of Our Investigations

At the hospital and outpatient clinics of the University of Colorado Medical Center, we have determined the doses administered to the body and to the gonads of patients during some of the more common x-ray examinations (table 1). Measurements also revealed that during fluoroscopic examination of an infant the skin in the central beam may receive as much as 5 r per minute (table 2). Unless fluoroscopic examination of a small infant is done with the shutters especially carefully closed to limit the size of the field only to that unavoidable minimum required for adequate examination, the dose will be given to almost the whole body of the infant and will include critical areas, as the gonads and thymus.

Means for reducing radiation doses received by the patient during x-ray examinations also were studied. The reduction of the exposure dose to the part and to the gonads can be achieved ideally:

1. By reducing the number of examinations to those essential for the proper medical care of the patient.

2. By developing roentgenologic technics with enhanced efficiency, as, for example, by intensification of the fluoroscopic and roentgenographic images. Currently available image

TABLE 1

DOSE RECEIVED BY PATIENTS DURING X-RAY EXAMINATION

EXAMINATION	VIEW	DOSE IN MILLIROENTGENS		
		To skin at central beam	*To male gonads*	*To female gonads*
Chest (72 in.)	Posteroanterior	35	0.04	0.3
Chest (72 in.)	Lateral	115	0.14	1.3
Abdomen	Anteroposterior	1330	125	250
Lumbar vertebrae	Anteroposterior	1330	125	250
Abdomen	Lateral	6200	172	1000
Lumbar vertebrae	Lateral	6200	172	1000
Pelvis	Anteroposterior	1500	1100	900
Intravenous pyelography	Five films	6650	2400	2000
Roentgenographic pelvimetry	Two films	8860		2150
Thoracic vertebrae	Anteroposterior	1330	1.7	28
Chest (photoroentgenography)	Posteroanterior	870	0.73	15
Chest (photoroentgenography)	Lateral	1560	3.3	24
Femur		485*	45*	11*
Leg		16*	0.07*	0.07*
Cervical vertebrae		445*	0.25*	0.95*
Skull	Posteroanterior	1250*	0.25*	0.40*
	Lateral	480*	0.20*	0.25*
	Occipital	1250*	0.25*	0.40*
Esophagus, stomach and duodenum	Oblique and lateral	2150†	112†	560†
	Anteroposterior	530†	112†	560†
	Fluoroscopy (4 to 6 min.) and spot films	34,000 to 52,000	10 to 15	24 to 36
Barium enema	Oblique and posteroanterior	1540†	210†	430†
	Anteroposterior	530†	210†	430†
	Fluoroscopy (3 to 5 min.) and spot films	25,000 to 43,000	95 to 160	750
Chest fluoroscopy in Rheumatic Fever Clinic (1 min. average)		3000	0.8	0.5‡

*Per view.

†Overhead film only.

‡Estimated.

intensifiers can reduce the exposure dose for certain examinations by operation at a fraction of the usual milliamperage required. There is an imperative need for better intensifiers that will permit the examination of larger fields than is now possible.

3. By developing screens and films of increased sensitivity which will require less radiation to produce images of diagnostic quality. Many companies are presently devoting much time and money to achieve these goals.

There remain certain simple and readily

TABLE 2

DOSES RECEIVED BY INFANTS DURING FLUOROSCOPY*

FLUOROSCOPY	DOSE TO SKIN AT CENTRAL BEAM *(Milliroentgens per minute)*	DOSE TO GONADS IF NOT COVERED BY SHIELD *(Milliroentgens per minute)*	
		Male	*Female*
Chest	2500 to 5000	Gonads not in the direct beam	
		1.8	0.9
		Gonads in the direct beam	
		1800	900
Abdominal	2500 to 5000	1800	1500

*The data in this table are based on measurements on an infant cadaver. Table top-tube distance, 18 in.; filter, 2 mm. aluminum.

available measures which we have found practical and effective for the reduction of exposure dose during essential x-ray diagnosis. These are:

1. Use of a 2 mm. aluminum filter over the tube ports. Trout, Kelley and Cathey[5] have thoroughly discussed the reduction of exposure dose to parts in the useful beam by addition of an aluminum filter to the x-ray tube.

2. Use of cones or diaphragms to limit the field size as nearly as possible to the part being examined.

3. Use of ordinary leaded aprons or something similar to shield the parts of the body not being examined when the patient is in the horizontal position.

4. Interposing a sheet of lead, 1/16 in. thick, vertically between the tube and the patient's pelvis during examinations when the patient is standing, as in examination of the chest when the target-to-film distance is 72 in.

The efficiency of some of these measures in reducing the gonadal exposure dose is illustrated in table 3.

Comment

The numerical results we have presented may be subject to great variations because of differences in the body dimensions of various patients, differences in the x-ray generating equipment, differences in collimating and shielding devices and technics, and possibly as a result of other factors. The technical details of how our measurements were made have been described in another article.[6] Our results agree approximately with similar data obtained by Ardran and Crooks,[7] Billings, Norman and Greenfield,[8] Webster and Merrill,[9] and Stanford and Vance.[10] We have made only a limited study of the exposure dose received by the gonads of children, but the indications are that the hazard of such exposure may be considerably higher for children than for adults. This deserves more detailed study.

Recently published data[8] have indicated that the gonadal exposure dose in certain examinations is zero. Such data are misleading and unenlightening. It is better to state the estimated dose as a number, however small it may be, than to express it as zero. Zero multiplied by a large number is zero. However, multiplication of a small finite number by a very large number results in an appreciable product, such as the total gonadal dose received yearly by the population of the United States.

Although intravenous pyelography, x-ray pelvimetry, barium-enema examinations, and examinations of the lumbar vertebrae, abdomen, gallbladder and upper part of the gastrointestinal tract comprised only 20.4 per cent of the total number of x-ray examinations, they were responsible for 81.5 per cent of the total gonadal exposure dose received. On the other hand, examinations of the chest comprised 45.5 per cent of the total number of examinations, but accounted for only 0.2 per cent of the total gonadal exposure dose re-

TABLE 3

EFFECTIVENESS OF COLLIMATING DEVICES IN REDUCING ADULT GONADAL EXPOSURE DOSE

EXAMINATION	DEVICE	DOSE TO MALE GONADS		DOSE TO FEMALE GONADS	
		Milliroentgens per film	*Per cent*	*Milliroentgens per film*	*Per cent*
Chest (posteroanterior; 72 in. F.F.D.; 86 peak kilovolts; 10 milliampere seconds)	None	0.70	100		
	Videx adjustable round lead diaphragm	0.080	11		
	Videx plus lead screen shielding the patient outside the field to be visualized	0.070	10		
	Lead screen shielding the patient outside the field to be visualized; no diaphragm	0.19	27		
Chest (anteroposterior tomography; 30 in. F.F.D.; 56 peak kilovolts; 60 milliampere seconds)	No cone, diaphragm or shield	3.2	100	1.7	100
	Lead apron shielding patient outside the field to be visualized	0.34	11	0.17	10

ceived by the patients. Pelvimetric examinations comprised 0.6 per cent of the total number of examinations and accounted for 4.5 per cent of the total gonadal dose received. An additional consideration in x-ray pelvimetry is that at least a part, and sometimes all, of the dose is given simultaneously to two persons, namely, the mother and the fetus. If protective devices had not been used in all of these x-ray examinations, the gonadal exposure doses would have been considerably higher than they were (table 3).

Although protective devices are of limited value in cases in which exposure of the gonads to radiation is unavoidable, as, for example, in cases in which bony pelvis is under scrutiny, they should be used with strict consistency in all cases in which unobstructed view of the gonadal region is not required. The use of such devices has not caused any inconvenience to our patients or to ourselves.

One of the reasons for making this study was to provide physicians who order x-ray examinations with information about the genetically effective gonadal dose received during a particular examination. We believed that this information would enable the physicians to weigh the possible, long-term consequences of such a dose against the necessity of obtaining the desired information. It was hoped that this information would result in the elimination of some unessential x-ray examinations. This hope has been realized, for the number of requests for x-ray pelvimetry and infant fluoroscopy has been reduced significantly.

Another reason for this study was to compare the average gonadal exposure dose received by patients observed at the University of Colorado Medical Center with the recommendation of the Committee on Genetic Effects of Atomic Radiation of the National Academy of Sciences.[4]

In the year covered by this study, all patients observed at the Medical Center received an average gonadal exposure dose of approximately 0.25 r per year per person (table 4). This is of the same order of magnitude as the reasonable quota of 10 r to the reproductive

TABLE 4

AVERAGE YEARLY GONADAL EXPOSURE DOSE RECEIVED BY PATIENTS SERVED AT UNIVERSITY OF COLORADO MEDICAL CENTER*

Estimated number of persons under 30 depending on this hospital for medical care	100,000
Estimated number of patients served during the year	36,300
Number of patients examined with x-rays	6,813
Total number of x-ray examinations	27,674
Number of x-ray examinations on males	13,560
Number of x-ray examinations on females	14,114
Weighted average gonadal exposure dose per examination	
For all patients examined	0.3 r
For males examined	0.2 r
For females examined	0.4 r
Total gonadal exposure dose for all patients examined	9250 r
Total gonadal exposure dose for all males examined	3200 r
Total gonadal exposure dose for all females examined	6050 r
Estimated average gonadal exposure dose per patient served per year (including patients who were not examined with x-rays)	0.25 r
Estimated average gonadal dose per year per person under 30 depending on this hospital for care	0.1 r

*From January 1, 1955 to December 31, 1955, inclusive.

cells of the general public of the United States (not to be exceeded during the reproductive age up to 30 years), according to recent recommendations of the National Committee on Radiation Protection and Measurement[11] and the Genetic Committee of the National Academy of Sciences.[4] These committees have recommended that, in the first 30 years of life, the general population of the United States should not receive a total gonadal exposure dose of more than 10 r per person as a result of medical x-ray examination. This is a reasonable, but admittedly not a harmless, dose. At the request of the physicians who order x-ray examinations, the Department of Radiology of the University of Colorado Medical Center is subjecting the segment of population depending on the Center for its medical care (currently, patients less than 30 years of age) to a gonadal dose in the neighborhood of 1 r per reproductive lifetime.

Hazards to professional personnel result chiefly from the use of uncalibrated or obsolete apparatus in poorly designed, inadequately shielded rooms, or from carelessness. These hazards can be reduced to safe levels by complying with the recommendations of the National Committee on Radiation Protection.[12] The walls of new laboratories should be constructed and shielded according to the recommendations of this committee. Old buildings should be surveyed by a competent physicist or inspector, and, if needed, enough lead should be added to the walls to protect persons who are unavoidably exposed.

Permanent records should be maintained of the doses received by technicians in the performance of their duties, and supervisors should insist on safe technics and habits. Weekly doses received by technicians never should exceed the permissible doses recommended by the National Committee on Radiation Protection.[13]

The wearing of film badges or ionization chambers for monitoring doses is still an imperfect way to measure doses absorbed. Nevertheless, these devices are of inestimable value for making personnel safety-conscious, and for this reason alone they should be worn at all times while the workers are on duty. Furthermore, they may be valuable records in the medicolegal evaluation of claims against the employer for supposed radiation damages received by the employee.

Periodic health examinations should be made on all employees, and the records permanently maintained. Particularly important are pre-employment examinations including

data on the blood count. Persons in poor health should not be assigned work in radiology departments. Month-long vacations for x-ray and other radiation workers have been advised. Vacations, however, are not to be considered protection against or a compensation for overexposure.

Physicians and technicians should never hold patients or remain in the room with operating machines without the protection of adequate shields, aprons and gloves. Controls should be shielded so the operator is protected from both direct and scattered rays. Professional personnel should not hold films or place parts of their body in the beam during fluoroscopy or filming under any circumstances without adequate shielding, and then only when absolutely essential to the proper medical care of the patient. Persons who are not radiation workers may be allowed to hold patients occasionally.

Special care must be taken during examinations with portable machines in rooms where there are inadequate arrangements for protection. Gloves and aprons should be worn by the technician. Long switch cords should be used since they permit the operator to make exposures when standing at least 6 ft. from the tube and patient.

The rotation of personnel through fluoroscopic duties is recommended, especially if the work schedule is heavy and if appreciable exposures *below* permissible levels are being received.

In all metropolitan centers there are qualified persons capable of inspecting conditions in x-ray departments, and their services usually can be secured for inspections even in remote rural areas. All x-ray installations should be inspected yearly for health safety as well as for medicolegal reasons, and the results of the inspection should be recorded.

It is reasonable to anticipate that in the near future the recommendations outlined, or similar ones, for the safety of radiation workers will become legal requirements in all the states. In fact, the recommendations of the National Committee on Radiation Protection[12] now are legal requirements in several states, including Pennsylvania and Texas.[14]

Conclusions

1. Exposure of large numbers of the population to x-rays and other mutagenic agents is increasing, and the resulting mutations are harmful.

2. All persons who use these agents or who are exposed to them should seek to reduce the exposure hazards.

3. Exposure doses received by patients undergoing x-ray examinations in a typical x-ray department are given in a tabular form and analyzed as to the comparative hazards of different types of examinations.

4. The average gonadal dose due to medical x-rays received during the reproductive lifetime of the segment of population served by one typical hospital (University of Colorado Medical Center) under the present conditions is of the order of magnitude of 1 r per person per reproductive lifetime. This is compared with the recommendations of the National Academy of Sciences and of the National Committee on Radiation Protection, which call for an average dose of less than 10 r to the gonads of the population of the United States from medical x-rays taken during the 30 years of reproductive life.

5. Measures to be taken in order to reduce the gonadal dose during diagnostic x-ray examinations are discussed and illustrated by actual data.

6. X-ray examinations in which the diagnostic benefit outweighs the hazard are the only justifiable examinations. Fortunately, the benefit outweighs the hazard in most examinations which are done in the x-ray department of a hospital in which the staff members are aware of the actual doses received during the performance of the x-ray examinations they order.

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Books Received

Books received are acknowledged, and, as space permits, those of principal interest to our readers are reviewed more extensively. Reviews appear in this issue starting on page A-154; additional listings are on pages 282 and A-164.

Pathogenesis and Treatment of Parkinsonism. Sixth annual scientific meeting of the Houston Neurological Society. Compiled and edited by William S. Fields, M.D., Professor and Head, Division of Neurology, Baylor University College of Medicine, Houston, with 24 contributors. 372 pages, illustrated. 1958, Charles C Thomas, Springfield, Illinois. $10.75.

Anatomy for Surgeons; the Back and Limbs. By W. Henry Hollinshead, Ph.D., Professor of Anatomy, Mayo Foundation, and Head, Section of Anatomy, Mayo Clinic, Rochester, Minnesota. Vol. 3. 901 pages with 785 illustrations. 1958, Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York. $23.50.

Pulmonary Circulation. An international symposium sponsored by the Chicago Heart Association. Edited by Wright R. Adams, M.D., Professor and Chairman, and Ilza Veith, Ph.D., Associate Professor of the History of Medicine, Department of Medicine, University of Chicago, the School of Medicine, Chicago, with 35 participants. 316 pages, illustrated. 1959, Grune & Stratton, Inc., New York and London. $4.50.

Staphylococcal Infections. By Ian Maclean Smith, M.D., Assistant Professor and Chief, Infectious Disease Division, Department of Internal Medicine, State University of Iowa, Iowa City. 180 pages. 1958, The Year Book Publishers, Inc., Chicago. $4.25.

Diseases of the Nervous System. By Sir Francis Walshe, M.D., Consulting Physician, University College Hospital, London, England. Ed. 9. 373 pages with 60 illustrations. 1958, E. & S. Livingstone Ltd., Edinburgh and London. Distributed by The Williams & Wilkins Company, Baltimore. $8.00.

Clinical Obstetrics and Gynecology. A quarterly book series. Symposium on Special Diagnostic Aids. Edited by C. Paul Hodgkinson, M.D., Gynecologist-Obstetrician-in-Chief, Henry Ford Hospital, Detroit. Symposium on Abnormal Uterine Bleeding. Edited by John I. Brewer, M.D., Professor of Obstetrics and Gynecology, Northwestern University Medical School, Chicago, with 44 contributors. Vol. 1, No. 3. 1958, Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York. $18.00 per year.

The Indian Year-Book of Medical Sciences (1958). Edited by Madhusudan M. Desai, M.D., Dhirubhai V. Doshi, M.R.C.P. and Noshir H. Wadia, M.D. 483 pages, illustrated. 1958, Current Technical Literature Co., Private Ltd., Bombay. 75 shillings.

Basic Issues in Psychiatry. By Paul V. Lemkau, M.D., Professor, Public Health Administration, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore. 106 pages. 1959, Charles C Thomas, Springfield, Illinois. $3.50.

Poliomyelitis. Proceedings of the fourth International Poliomyelitis Conference. 684 pages with 422 illustrations. 1958, J. B. Lippincott Company, Philadelphia and Montreal. $7.50.

Psychopathic Personalities. By Professor Kurt Schneider, formerly, Director, Psychiatric and Neurological Clinic, University of Heidelberg, Heidelberg, Germany. Translated by M. W. Hamilton, B. A., Tutor for Psychiatric Social Work, Department of Psychiatry, University of Manchester, Manchester, England. Ed. 9. 163 pages. 1959, Charles C Thomas, Springfield, Illinois. $3.75.

Differentialdiagnose Innerer Krankheiten. By Robert Hegglin, M.D., Professor of Internal Medicine, University of Zurich, Zurich, Switzerland. Ed. 6. 819 pages with 517 illustrations. 1959, Georg Thieme Verlag, Stuttgart, Germany. Distributed in the United States and Canada by Intercontinental Medical Book Corporation, New York. $18.95.

Juvenile rheumatoid arthritis occurs most frequently between the ages of two and five years. Early clinical manifestations include daily high fever, rash, arthralgia, cardiac involvement, pulmonary inflammation, severe abdominal pain and rare systemic conditions. Arthritis may occur at any time. The cause of the disease is still unknown, and no specific diagnostic test has yet been devised. All drugs used in treatment are palliative; preservation of normal motility, good nutrition and emotional well-being are most important in the therapeutic regimen.

Juvenile Rheumatoid Arthritis: Challenges and Pitfalls in Diagnosis and Treatment

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AN editorial published in this journal[1] called attention to the persistence of many unsolved problems relating to critical human diseases. The editor expressed his belief that progress toward solution of such clinical problems may be encouraged by frequent inventories of available knowledge, and also by re-evaluation of evidence on which this knowledge (of the cause, pathology, diagnosis, treatment and prevention of a disease) is based.

To those concerned with chronic disease in children, juvenile rheumatoid arthritis presents many unsolved problems. An attempt will be made here to survey current knowledge, with the hope that investigative interest of clinicians and laboratory workers may be aroused, leading thereby to improved methods of caring for these young patients.

Most of the recent medical literature concerning rheumatoid arthritis has been written by specialists whose experience has been gained in arthritis clinics where patients of all ages are seen. When viewed as a segment of this total arthritic population, children very likely represent less than 5 per cent of the patients.[2] However, to conclude from this information that the disease rarely occurs in children would be erroneous. To be sure, chronic debilitating diseases are fortunately less common during childhood than during later life. Available statistical data indicate that the incidence of new cases of rheumatoid arthritis is probably about 2.7 per 100,000 children under the age of 15 years.[3] This figure is comparable to the incidence of the nephrotic syndrome in children (2.3 per 100,000 under 10 years of age),[4] and of juvenile diabetes mellitus (less than 2.8 new cases per 100,000 under 15 years of age),[5] both of which dis-

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eases are of major interest to physicians charged with care of children.

Juvenile rheumatoid arthritis commands medical attention not only because of its comparatively common occurrence but also because of its chronicity, its effect on growth and maturation, and the socio-economic problems it presents to the patients' families, physicians and communities.

Clinical Manifestations

Rheumatoid arthritis at any age should be viewed as a generalized systemic disease of unknown cause and pathogenesis involving acute and chronic inflammation of perivascular connective tissue. By definition, major inflammatory activity involves the joints at some time during the course of the disease, but skeletal musculature, heart, lungs, brain, lymphatics and skin may also be affected. As they do in response to most inflammatory processes, children tend to show more vivid systemic reactions to rheumatoid arthritis than do adults. Fever, severe malaise, anorexia and weight loss are common during active phases of the disease. Normal skeletal growth may be interrupted, and anemia may be severe.

The disease can begin at any age, even in the first year of life. Most commonly it starts between the ages of two and five years (whereas acute rheumatic fever is comparatively rare among preschool children). Especially in these younger children, generalized inflammatory features of the disease may appear weeks or months before gross signs of arthritis. These acutely ill patients always are challenging differential diagnostic problems. Unless the possibility of acute "rheumatoid disease"[6] is considered, the cause of the illness may remain a perplexing mystery in spite of elaborate, extensive and expensive laboratory investigations. For this reason it seems desirable to comment briefly on certain early manifestations which should strongly suggest the presence of acute rheumatoid arthritis in its prearthritic phase.

Fever is frequently the manifestation which causes parents to bring the child to a physician. Daily spiking temperatures to 104 or 105° F. per rectum are common. Careful examination may reveal signs suggesting mil upper respiratory infection and moderate lyn phadenopathy, but fever persists despite i tensive therapy with salicylates or antibiotic or both. Febrile convulsions are fortunatel rare. During febrile periods, which occur mor often during evening hours, the child may b extremely irritable and restless, only to re sume normal behavior as his temperature re turns toward normal. The disturbing diagnosi of "fever of unknown origin" is often applie to these children for many months, until char acteristic changes in the joints appear.

Rash should be searched for during febril periods. Along with fever, 75 to 80 per cent of patients with acute rheumatoid disease display a fleeting, salmon-pink, discrete, maculopapular, nonurticarial rash, often distributed widely over the entire body surface but tending to concentrate on skin overlying the large joints of the extremities. These skin lesions tend to appear circular, or to be arranged in circinate fashion, the diameter of a circle being no more than about 1.0 cm. The rash commonly erupts during febrile periods and disappears as the temperature falls. It is just as characteristic of acute rheumatoid arthritis as is the erythema marginatum of acute rheumatic fever. If this rash is seen, or reported by reliable parents, the physician may be able to reduce the number of laboratory studies for such a febrile child.

Arthralgia may also be present during this early phase of the disease, without overt signs of acute inflammation of the painful joints. Any joint or combination of joints may be involved. The pain often comes and goes along with fever and rash. Many of these small children manifest their arthralgia by refusing to walk or refusing to use an arm for self-feeding, until the pain subsides in a day or two. Others tend to be irritable and slow to embark on their usual play activity after arising in the morning or after naps, a symptom which resembles the "morning stiffness" Cobb and co-workers[7] described in adult rheumatoid patients.

Cardiac involvement occurs more frequently in juvenile rheumatoid arthritis than is generally realized, and may even initiate the dis-

ease. Pancarditis is to be expected. Pericardial friction rubs, cardiac valvular murmurs, and evidence of myocardial insufficiency may all be found. The diagnosis of acute rheumatic fever is apt to be seriously entertained. However, the electrocardiogram does not reveal prolongation of the P-R interval in cases of rheumatoid carditis, as one expects to find in severe rheumatic carditis. Acute carditis accounts for a large proportion of deaths from rheumatoid arthritis in children. Digitalis and its derivatives are of doubtful therapeutic benefit. Treatment with ACTH or an adrenocorticosteroid is often dramatically effective. The prognosis for the heart is excellent if the patient survives the acute episode. Clinically detectable permanent cardiac damage rarely occurs.

Pulmonary inflammation, including both pleuritis and pneumonitis, frequently accompanies cardiac involvement but may also occur independently. Physical findings tend to be more conspicuous over the lower pulmonary lobes. Roentgenograms of the chest do not always reveal the severe degree of pneumonitis suggested by clinical signs. Findings tend to persist for months before resolving, and are unresponsive to antibiotic therapy. Pathologic study of such lungs has shown well-defined fibrinoid necrosis between pulmonary alveoli.[8]

Severe abdominal pain, which may suggest acute appendicitis or peritonitis, can complicate the clinical picture. Mesenteric adenitis may explain this symptom. The generalized systemic nature of the disease increases surgical risk, so that laparotomy should not be performed unless signs of local disease are extremely compelling.

Rarer systemic manifestations of acute rheumatoid arthritis include chorea, iridocyclitis and band-shaped keratitis, and subcutaneous nodules. Hemorrhage into the skin, or from the bowel or urinary tract, is rarely, if ever, seen.

Arthritis, with redness, heat, swelling and tenderness, may be present at the onset of the disease or may not be evident until months after systemic inflammatory activity has been experienced. Indeed, in some children arthritic changes develop insidiously without any of the systemic accompaniments described. Initially, only a single joint, such as a knee, may be swollen and painful. Involvement of the cervical spine is common. Fusiform swelling of proximal interphalangeal joints of the hands usually occurs sooner or later. The character of the polyarthritis does not differ significantly from that in adult rheumatoid patients, and should never be difficult to recognize. The correct diagnosis becomes obvious at this point in the course of the disease.

The responsible physician now sheds his anxiety relating to the differential diagnosis suggested by whatever combination of alarming systemic signs and symptoms may have preceded the appearance of characteristic rheumatoid changes in the joints, only to acquire a new set of problems relating to proper therapeutic management.

Etiologic Hypotheses

The cause of rheumatoid arthritis is still unknown. Climatic influences, foci of infection, hereditary predisposition, emotional imbalance, and nutritional deficiencies have all been seriously considered as causative factors. All of these occasionally seem to influence the course of the disease. However, convincing evidence that any of these factors initiate the process has not been offered. A word of caution is in order at this point. Well known to all students of the disease is its tendency to remit and exacerbate spontaneously. Any newly introduced therapeutic agent or change in environment may be falsely credited for producing improvement if judgment is based on a single case. Clinical investigation of etiologic and pathogenetic aspects of this disease is fraught with hazards which demand rigid control and careful statistical scrutiny.

Investigative interest currently focuses on two possible etiologic factors. Stetson[9] recently summarized the current status of knowledge concerning peculiar dissociants of bacteria known as L forms (pleuropneumonialike organisms). In the presence of unfavorable environmental conditions, many types of bacteria, including the streptococci, are able to shed their capsules, cell walls and most of

their cytoplasmic constituents and to exist as free-living, slowly reproducing genetic material consisting almost solely of nucleoprotein. When environmental conditions improve, these L forms can and do revert to their previous specific bacterial forms. Intricate special cultural methods are needed to demonstrate L forms in the laboratory.[10] It is possible that nucleoprotein L forms and rheumatoid arthritis may be related etiologically in a manner similar to the well-established but poorly understood relationship between beta hemolytic streptococci, rheumatic fever and hemorrhagic glomerulonephritis.

A large group of enthusiastic workers is presently investigating the possibility that auto-immune mechanisms are responsible for rheumatoid arthritis. The concept of renal auto-immunization is well established in experimental glomerulonephritis. Glynn and Holborow[11] have been able to produce arthritis in rabbits by the combined effect of tissue polysaccharide obtained from human costal cartilage plus heat-killed group A beta hemolytic streptococci. At least two aspects of the disease in humans would seem to argue against present-day auto-antigenic theories. Agammaglobulinemia recently was reviewed in this journal.[12] The authors of that paper also reported that rheumatoid arthritis occurs with unexpected frequency among patients who have either congenital or acquired agammaglobulinemia.[13]

Another conflicting finding relates to the concentration of complement in the serum of rheumatoid patients. Complement is presently viewed as a complex of factors required to permit completion of many antigen-antibody reactions. Wedgwood and Janeway[14] reported that serum complement titers of children with disseminated lupus erythematosus, acute glomerulonephritis and the nephrotic syndrome are lower than normal, a finding which would be anticipated in the presence of a classic antigen-antibody reaction. Children with rheumatoid arthritis were found to have high titers of serum complement, however, and these titers fell toward normal during remissions induced by treatment with ACTH. Other workers have reported similar alterations of complement levels in adult rheumatoid patients.

The acuteness and dramatic severity of the onset of rheumatoid disease in many of the afflicted children suggest that they may provide a fertile field for investigation of these possible etiologic mechanisms.

Aids in Diagnosis

Certain clinical observations already mentioned should lead the physician to consider the possibility of rheumatoid arthritis. High spiking fever unresponsive to therapy with salicylates and antibiotics is perhaps the most impressive clue. Typical rash and transient migratory polyarthralgia during febrile periods may also support the diagnosis.

A normocytic, normochromic anemia is usually present, and it responds poorly to treatment with iron and vitamin supplements during active phases of the disease. Moderate polymorphonuclear leukocytosis is common. The erythrocyte sedimentation rate is very rapid (often over 100 mm. per hour) during periods of febrile activity. "Acute phase reactants" such as C-reactive protein, serum mucoprotein, and serum tyrosine are also present in high concentration, and the total serum globulins are occasionally increased. Elevation of the antistreptolysin-O titer is unusual.

Search for the so-called rheumatoid factor in the serum by means of the sheep cell agglutination test or the latex fixation test has yielded negative results in the vast majority of children studied. The reason for this difference between juvenile and adult rheumatoid patients is unknown.

By the time joint changes are visible roentgenographically and synovial tissue biopsies show the chronic inflammatory reaction consistent with rheumatoid arthritis, the diagnosis is usually obvious. These studies rarely have crucial diagnostic value, although they may be useful as methods of objectively documenting the course of the disease and responses to various forms of treatment.

Still needed is a specific diagnostic test.[15] Progress in serologic study of the disease has been rapid during the past decade and should eventually yield the desired diagnostic tool. Until this is available, diagnosis must be

based on clinical observations, usually spanning a considerable length of time.

Approach to Therapy

Before the physician embarks on any regimen of treatment he should recall that he, the child and the parents face a long-range, highly unpredictable problem. Periods of spontaneous remission are common and may always be anticipated hopefully. Discouraging exacerbations are equally characteristic. Active disease may last only a few months or may persist as long as 40 years. Present knowledge offers no reliable prognostic clues to enable the physician to foresee a patient's future course. Death may occur during a period of severe systemic activity. Although the arthritis itself is not fatal, progressive skeletal deformities, muscular contractures and weakness, and nutritional disturbances secondary to chronic inflammatory disease may lead to disastrous physical and emotional crippling.

Any therapeutic regimen should have clearly defined goals. From the broadest aspect, the goals of treatment for the juvenile rheumatoid patient should include (1) preservation of mobility and self-sufficient independence insofar as this is medically possible, (2) maintenance of good nutritional status and promotion of normal physical growth, and (3) support and encouragement of the patient's normal intellectual, behavioral and social development, in close cooperation with parents and appropriate social agencies.

Short-range goals which should also influence choice of treatment include (1) relief of pain, (2) modification of fever, (3) prevention of muscle weakness, contractures and bony ankyloses, (4) avoidance of environmental experiences which may precipitate exacerbations, such as intercurrent infections, trauma and emotional upsets, and (5) avoidance of iatrogenic complications which may create more serious problems than those for which treatment was prescribed, this being the most important goal of all.

Therapy

The literature relating to treatment of rheumatoid arthritis is immense in both scope and diversity. Whenever a variety of agents and technics is advocated, therapeutic confusion is a potential hazard. Retreat to a nihilistic attitude is also dangerous. An appeal for conservatism in the care of these children, based on the goals which have been proposed, is the keynote of this paper.

Attention is directed to the series of papers which have recently appeared in this journal concerning general and specific therapeutic measures,[16] proper use of preventive and rehabilitative physiotherapy,[17] and the emotional aspects of physical disability which require medical attention.[18] Statements made by the authors of these papers are generally applicable to juvenile patients.

Most useful for treatment of the disease during phases of intense activity are the adrenocorticosteroids and their analogues. Dosage must be decided empirically and re-evaluated frequently in an effort to achieve the smallest daily dose which will permit general comfort and musculoskeletal activity. Especially when all signs and symptoms of the disease have been masked by steroid therapy, reduction of the dose should be attempted. Otherwise, the onset of a spontaneous remission may go unrecognized.

Well known are the undesirable side effects of the adrenocorticosteroids which resemble Cushing's syndrome. These may ultimately force discontinuation of treatment despite persistence of active rheumatoid disease. Less attention has been paid to reports that prolonged administration of adrenocorticosteroids may convert rheumatoid arthritis to the classic picture of periarteritis nodosa[19] or to disseminated lupus erythematosus[20] by mechanisms which are unknown. Certainly the steroids should be viewed as highly potent pharmacologic agents to be used only when their potential benefits clearly outweigh all known hazards.

Phenylbutazone has been effective in about 50 per cent of the juvenile cases in which it has been tried. A total daily dosage of 200 to 400 mg. divided into three or four equal portions will usually produce symptomatic improvement if the agent is to be effective at all. Because it does not possess adrenocortical ac-

tivity and does not influence adrenocortical secretion, the usual precautions should be taken to avoid an addisonian crisis if therapy is being changed from a steroid drug to phenylbutazone.

Chloroquine is a promising agent in adults. Unfortunately this drug is commonly available only in a 250 mg. enteric-coated tablet, and the daily dosage recommended for treatment of adult rheumatoid patients is 250 mg. Experience with this agent among juvenile patients is therefore limited.

Salicylates, even in maximal dosage of about 100 mg. per kilogram per day, do not affect fever and have little effect on arthritis, but may occasionally provide adequate symptomatic relief.

One must be constantly mindful that no pharmacologic agent currently available can cure rheumatoid arthritis. All drugs are palliative. More important at every phase of the therapeutic regimen is preservation of normal mobility, good nutrition, and emotional well-being by traditional methods.

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The family physician must summon all his skill as a counselor when he delivers a deformed or mentally defective child or is consulted about mental retardation. To aid the physician in this problem, the author points out various abnormalities of the newborn, indications of delayed development, and causes of mental and pseudomental deficiency. He also discusses the role of genetics in mental deficiency and reviews answers to questions commonly asked by parents of mentally retarded children.

The Family Physician and the Mentally Retarded Child

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In general medicine as in pediatrics, the nature of practice has changed fairly rapidly in a generation. Less and less time is spent in treating acute infections and their sequelae, and more on diagnosis and management of anomalies and handicaps. In this connection, the physician must become a counselor to the family. In some instances, the family and afflicted child can be referred to a surgical specialist, as in the case of congenital heart disease. If, however, there is no present treatment, as in cases of mental deficiency, the physician cannot simply present the family with the diagnosis and send them away. Parents expect the physician to have knowledge and advice of kinds not fully covered in medical school curriculums. Physicians should not leave the parents to the care of semiprofessional counselors, but rather should, I believe, accept the role of chief counselor, enlisting help from specialties as needed.

All of the family physician's art and skill as a counselor will be called on when he delivers a deformed or obviously mentally defective child. The latter would be a child with marked microcephaly or macrocephaly, or a child who had unmistakable stigmata of mongolism. Other types of congenital mental deficiency may not be obvious until weeks or months after birth. Other anomalous conditions (not commonly associated with mental retardation), such as clubfoot, congenital heart disease, harelip, or even myelomeningocele, at least carry with them the possibility or probability that something can be done to correct the situation.

In the case of mongolism or extreme microcephaly, it is rather evident from the beginning that the child's future, so far as mental development is concerned, can never be normal. The physician can do much to help the family in this tragic situation. That he can fail

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to be as helpful as he might, or even, sometimes, may add to the family's confusion and prolong the time when an accurate diagnosis and acceptable plans for the future can be made is, of course, entirely possible. Accurate diagnosis of congenital defects during the early neonatal period has been made more difficult by the fact that the time the newly born infant spends in the hospital has been progressively decreased until it is only a few days in most instances. This means that in a week or less the physician and his professional assistants, including house officers and nurses, have a shorter time than formerly to decide whether the infant is, or is not, normal.

There are certain signs or symptoms which arouse the physician's suspicions. These include disproportion between the size of the head, usually the occipital-frontal circumference, and the length and weight of the child. These three measurements should be taken promptly on all newly born infants. Obvious deviations from normal, such as the signs of mongolism, microcephaly or macrocephaly, are usually rather obvious. However, it goes without saying that the physician must be as certain as he can that the child is, indeed, abnormal before he makes definite statements to this effect to the family. So long as he only suspects the presence of one of these abnormalities, the best course is to put a carefully worded note on the infant's chart with an outline of a definite plan to continue observations and to get consultation as needed to make a definite diagnosis before acquainting the parents with the strong probability of such a serious thing as mental defectiveness.

The intelligent mother notoriously expresses concern and asks for reassurance that her baby is entirely normal, often when there is not the slightest doubt in anyone's mind that this is the situation. If there is some doubt in the physician's mind but he does not wish to commit himself, he must be rather careful how he answers the mother's questions. I have had parents ask if I thought that their physician really knew that their child was not "right" but that he was afraid to tell them, or sometimes they are not quite so generous to their physician and ask bluntly, "Why didn't my doctor recognize this?" It often requires all of the art of the practice of medicine to avoid the appearance of inconclusiveness or evasiveness on the one hand and the unwarranted arousing of parental fears for the future development of their child on the other hand.

The unstigmatized child who later proves to be grossly mentally deficient may look as normal as another for the first days and weeks of life. Some of the signs which do occur shortly after birth may serve as a warning to the physician. These, of course, are failure of the infant to do those things which normal infants do, such as to cry, to suck and to feed normally. Conversely, the appearance of abnormal signs such as cyanosis, twitchings or frank convulsive seizures is ominous. However, these do not necessarily indicate that the central nervous system is abnormal or that it has been damaged beyond complete recovery. As all physicians know, a child may appear to be severely damaged following a long or traumatic birth only to recover completely without any subsequent demonstrable brain damage. As a matter of fact, this is the rule rather than the exception.

Growth and development during the first few weeks and months proceed rapidly, and the experienced physician should be able to recognize signs of delay of development by the time the child is three or four months of age. The intelligent and experienced mother will also have her suspicions aroused at about this time or shortly thereafter. For this reason, the monthly checkup should certainly include observations and a notation on the chart of the child's approximate developmental stage. One expects the child of one month to have gained approximately 2 lb. over his birth weight, to have gained 2 or 3 in. in length, to still retain the Moro and tonic-neck reflexes, and one is satisfied if the child makes any attempt at all to look at objects in front of him. At two months of age, he should be paying attention to his surroundings, to the extent that he will look at persons or objects directly in front of him and will follow to a limited extent as objects are moved laterally in his field of vision. He may not yet be able to turn his head to enable him to follow objects moving out of his field

of vision. Both the Moro reflex and tonic-neck reflex will be present, and he usually will have added another 1½ lb. at least to his weight.

By three months of age, he can look at objects near him and can follow an object moved through a circle of 360 degrees in front of him. As Gesell has said, he seizes objects with his eyes before he can seize them with his hands. As yet he knows no fear of strangers, and can be picked up by the physician without signs of alarm. It is probably too early for most mothers to detect signs of delayed development, but I believe that the physician may be able to do so if he has had much experience with infants, and I regard the eyes as the best indicator of the child's normal mental development. If I cannot get an infant to look at me as I examine him at three months of age, I am worried about his mental development or his eyes. The short attention span and lack of interest in his surroundings, so typical of the mentally retarded child, can be detected sometimes as early as three months of age.

By the time the child has reached four or five months of age, the mother will probably be aware of the fact if her child is not developing at somewhat near the normal rate. This is, of course, more likely to be true if she has other children. If she has not had experience in this connection, the child may well be six, seven or even eight months of age before the mother, through comparison with infants of her friends, realizes that her child is not coming along as rapidly as they are. She will hesitate at first to ask the physician, sometimes because she does not want to appear to be overly anxious and sometimes because she is afraid of the answer that she will receive. If she does raise questions about the child's development, I think that the physician must again be very careful of his answer unless he is absolutely sure of the situation. I do not think that he should put the mother off with some offhand statement to the effect that children vary so much in their development that comparisons are unwise and unfair.

A common bit of advice which may subsequently plague the physician is to the effect that "Your baby is doing just fine; give him time and he will be perfectly all right." This soothing statement may be exactly what is needed when the physician is convinced that the baby is, indeed, normal, and that the mother is overly apprehensive. However, if the mother's fears do prove to be well grounded and subsequent events prove that the child is retarded, the parents are very likely to remember the physician's words and to be critical of him. They may even conclude, rightly or wrongly, that the baby's development would have been better had the physician recognized the condition earlier and instituted treatment. It is well to remember that we have educated our patients to the general principle that a great many human ills can be bettered or cured if diagnosed early and given proper treatment. The mentally retarded child learns much during the preschool years, and early recognition of his condiiton may result in his getting special training, and may also prevent the development on the part of anxious parents of attitudes of rejection unfavorable to the child.

When the physician is consulted about the mental or physical growth of a child that he has not followed from birth, the diagnosis of mental retardation may be relatively easy, but the cause or causes and the best program to be instituted for the child and his family often take a considerable amount of thought and working out. The physician often has to call on certain medical specialists or other auxiliary services in order to get the best possible arrangement in such instances. Again, I would remind you that the physician is considered by his patients to have the ability to counsel on some matters that are not included in the curriculum of medical schools. For example, when a child is not doing well in school the physician is consulted. It seems to me that physicians not only should be able to check the child's vision and hearing and to determine in general if the child is physically able to enter into the school situation in a normal fashion, but they should also be able to advise the family what to do if it seems certain that the child's school troubles are due simply to a mental development incompatible with an education as it is offered in our public schools.

There is considerable confusion about one common complaint, namely, that the child has

TABLE 1

CAUSES OF MENTAL DEFICIENCY

I. Hereditary causes
  A. Several genes involved (common)
  B. Single genes involved (rare)
    1. Phenylpyruvic oligophrenia
    2. Galactosemia
    3. Tuberous sclerosis
    4. Cerebral angiomatosis
    5. Neurofibromatosis
    6. Sturge-Weber syndrome
    7. Friedreich's ataxia
    8. Laurence-Moon-Biedl syndrome
    9. Gargoylism
    10. Tay-Sachs disease (cerebral lipoidosis)

II. Prenatal causes
  A. Infection
    1. Syphilis
    2. Toxoplasmosis
    3. Rubella
  B. Iso-immunization (kernicterus)

III. Metabolic disorders
  A. Galactosemia
  B. Phenylpyruvic oligophrenia
  C. Hypothyroidism (poor prognosis)
  D. Hypoglycemia

IV. Other causes
  A. Mongolism (multiple causes; anoxia)
  B. Primary amentia

V. Cranial maldevelopment
  A. Microcephaly
  B. Craniostenosis
  C. Hypertelorism

VI. Cerebral injury
  A. Natal
    1. Hemorrhage
    2. Anoxia
    3. Subdural hematoma
  B. Postnatal
    1. Poisoning
    2. Infection
    3. Sequelae of infection

VII. Degenerative disorders
  A. Tay-Sachs disease
  B. Heredodegenerative disease
  C. Hurler's syndrome

TABLE 2

CAUSES OF PSEUDOMENTAL DEFICIENCY

Sensory defects
  Hearing defects
  Sight defects
  Language difficulties
  Aphasia
  Reading defects
Cerebral palsy
Chronic illness
Emotional disturbance
Psychosis (schizophrenia)
Unstimulated child (environmental retardation)

not yet learned to talk, or that his speech is defective. The easiest way for the physician to dispose of such a patient is to refer him to the speech correctionist, but I believe that we have failed our patients if the child's defective speech is a part of defective mental development, and it has been my experience that this is usually the case. The majority of children who are not talking by the time they are three, or who have grossly defective speech as they are about ready to enter school will also be found to exhibit other evidences of mental retardation. One exception to this statement is the emotionally upset child who, because of lack of proper care and stimulation or because of long-continued unfavorable emotional environment, has not developed speech in a normal fashion. Again, it should not require much questioning of the family concerning relationships among its members for the alert physician at least to suspect that the child's abnormal speech development is based on emotional disturbance or deprivation.

As I have indicated already, there is more than one reason for failure of mental growth and development to proceed in a normal fashion. In order that a correct and complete diagnosis may be made, the physician should keep in mind the various causes of mental deficiency and pseudomental deficiency. In its broader sense, the term pseudomental deficiency is used to designate the condition of a child who is not behaving in a normal manner at a given time, but who subsequently is not found to be mentally retarded. The various causes of mental deficiency and pseudomental deficiency are listed in tables 1 and 2. It is necessary for physicians to be as accurate as possible in making a diagnosis of mental deficiency if they are to be effective as counselors for their patients.

As I mentioned previously, when a physician is dealing with a child who appears to show evidence of mental retardation he will find it necessary to enlist the aid of other professional services. I have found the experienced psychologist of the greatest aid in help-

ing distinguish the mentally retarded child from the pseudomentally retarded one, and also to distinguish a child with a brain injury from the simple, genetically mentally inferior child. He can make this distinction with a high degree of accuracy by applying three or four standard psychometric tests as commonly used.

Often, the services of an otologist or ophthalmologist may be needed in order that the child's hearing or sight may be accurately evaluated. However, as part of his routine examination of the child even before one year of age, the general practitioner can be fairly certain whether or not a severe deficit in hearing or sight exists.

There are state and national agencies* on which the physician can call for help and advice to the parents of the blind or deaf preschool child. A great deal is lost if these defects are not recognized until the child is ready to go to school. Just like other children, they are capable of learning a great deal in the preschool period if properly handled. A somewhat similar situation exists with respect to the child who shows evidence of brain injury acquired natally or at some time during the postnatal period. Any physician can make a fair neurologic examination, but it is sometimes helpful to have a specialist as a consultant when the neurologic signs are not clear-cut or when their implications are confusing.

Today, most school systems have the services of a speech pathologist or speech correctionist. Many counties have such a consultant who spends a few hours a week in several different schools. This is very helpful for the school child with speech difficulties but, again, some help for the preschool child is often needed. Mention previously was made of the speech difficulties of mentally retarded children. However, there are others who have speech difficulties on an emotional basis. It is obvious that the child's speech should be as good as possible by the time he enters school, for the mere fact of defective speech will inevitably pose certain problems for the child and may result in emotional disturbances and a dislike for school.

There is one very important area where the family physician must assume to a certain extent the role of a psychiatrist. A physician's gestures and his words, even including their intonation, are of great import when a situation is one of counseling parents of a child who has a serious defect. It has been my experience that it is desirable to have more than one session with parents when the problem is one of counseling what to do in these tragic situations. Unless the family is especially well prepared, only a part of what is said at the first interview will actually get across, particularly when that part is to the effect that they have a seriously handicapped or defective child whose prognosis for normal growth and development is hopeless. It seems rather useless to attempt to go ahead and outline in detail just what will happen in the next several years. I say this because many of my patients come from considerable distances for consultation, and it is not easy for them to return several times. However, since these conferences in which the physician tries to impart to the distraught parents the exact nature of the child's defect and its implications for the future are very important, I think both the physician and the parents may well devote as much time as is needed to get these matters thoroughly understood.

It sometimes is advisable to have young parents bring along their parents to some of the counseling sessions; however, I try to emphasize to the father and the mother of the defective child that the problem is primarily theirs and one which they alone can decide, and that above all they must come to a decision which is acceptable to both of them; then they must stand firmly together against all others who would attempt to deter them from the course which seems best. All of us know

*Parents should write to their State Department of Health, Division of Maternal and Child Welfare, for information on state schools for children who are mentally retarded or otherwise handicapped. Parents of deaf children should write to the John Spencer Tracy Clinic, 924 West 37th Street, Los Angeles, California, for correspondence courses for deaf children of preschool age. The Volta Speech Association for the Deaf, 1537 35th Street, Northwest, Washington 7, D.C., also supplies pamphlets for parents of deaf children. The Lighthouse, 111 East 59th Street, New York, New York, supplies a manual for parents of blind children of preschool age.

how much help in-laws can be in such circumstances and also how much hindrance they can offer by such cruel remarks as "Nothing like this ever happened on our side of the family."

There has recently developed in many areas throughout the country a movement known as the NARC or National Association for Retarded Children. Branches of this organization are found in many towns and counties. The officers of the local chapter of the NARC often can perform a service for the parents of a defective child which the physician cannot offer. In my own area, I know that parents have had moral support from the local NARC members and that a program of parent education and mutual support goes forward. Often, such groups support day schools for the preschool child or for the school child who has been excluded from regular schools because of his severe mental deficiency. While these cooperative efforts seldom lead to very effective training or education of severely defective children, these day schools do serve the purpose of giving the mother some relief from the constant demands of her defective child and, in addition, the parents feel that the child is at least getting a chance to do whatever he can in a school situation. There is the added value of some degree of social maturity which might otherwise be denied the child who is excluded from school and largely from the play of normal children. Physicians can perform a service to such groups by giving talks when asked to do so, and, in general, serving in an advisory capacity. It is understood that the cooperative day school here mentioned is mostly for severely retarded children who cannot be educated but can assimilate training. The educable retarded child is admitted to special classes in most school systems.

Genetics and Mental Deficiency

A trained geneticist can be of great assistance to the physician and his patient, but this service usually is available only in connection with large medical centers. Most physicians must serve as their own geneticists and, fortunately, can do so because of excellent books which are available on the subject. Sometimes, it is possible to answer the anxious parents' question, "If we have other children are they likely to be similarly afflicted?" and to assure them that the defect under consideration is not hereditary. There are other cases, such as cases of cystic fibrosis of the pancreas, gargoylism, Charcot-Marie-Tooth type of muscular atrophy and many others, in which the physician cannot give a reassuring answer. To complicate the matter still further, there are, of course, certain manifestations which in one patient may be the result of heredity, in another the result of mutation, and, in still another, perhaps the result of nonhereditary injury of the fetus in the early course of development. Unfortunately for the physician who attempts to advise families in matters concerning the inheritance of defects, these are not transmitted in man in such a nicely predictable fashion as they are in inbred strains of laboratory animals.

It appears to be a conservative estimate that 60 per cent or more of mentally defective children are so because of heredity. Some investigators have placed this fraction of retarded children as high as 80 per cent of the total. It is true that environment is important in the mental growth and development of the child, but it is also true that the best environment can do no more than bring out the child's full potential. Conversely, it is true that the child with normal potential can achieve far less than he is capable of if he is in a highly unfavorable environment. It is also true that a child with normal or superior potential for mental development may have that favorable situation altered by natal or postnatal injury, usually by asphyxia, encephalitis, meningitis, intercranial hemorrhage, etc. Fortunately, the incidence of severe mental deficiency of the imbecile or idiot range is rare, probably no more than 5 per cent of the total.

The most standard and well-known example of mental deficiency is the child who suffers from what is ordinarily designated as mongolism, a term obviously applied because of his superficial resemblance to members of the Mongolian races. There is some evidence that mongolism may be inherited. I have seen several instances of two such children in one family, and there are in medical literature re-

ports of one or more instances of a woman, herself a mongoloid, giving birth to a similarly afflicted child. Sorsby said that the incidence of mongolism among the siblings of affected children is about 1 per cent. This seems to be due in part at least to the fact that the incidence of mongolism increases sharply with the age of the mother. Again, Sorsby is the authority for the statement that any woman who becomes pregnant after the age of 40 years runs a statistical chance of 1 to 6 per cent of having a mongoloid child.

The repeated occurrence of seriously defective children, including monstrosities, is not unusual. Yannet said, "Studies of pregnancies resulting in abnormal children, including the mentally retarded, have shown a significant incidence of such conditions as early maternal bleeding, suggesting imperfect placental attachments; toxemias of pregnancies, including eclampsia; and prematurity." Most physicians have had the experience of observing families in which two or more defective children are born. Murphy said that in families already possessing a malformed child the birth of a subsequent malformed offspring takes place with a frequency which is in the neighborhood of 25 times greater than that of the general population. He was not referring to mongolism specifically, but this same general rule holds. Others have estimated that the woman who has given birth to one mongoloid child runs a risk of as high as 1 to 20 that she may repeat. This is, of course, in very marked contrast to the incidence of mongolism in the population generally, which is approximately 1 per 800 births.

It is seldom safe for the physician to treat the matter of inheritance of defectiveness lightly with some such remark as, "This couldn't happen to you again in a million years," or some other nonscientific statement intended to reassure the parents unless, indeed, such is known to be the case. I think it is necessary to tell any parents of a defective child that the fact that they have produced a defective child, whether it be on the basis of genetics, iso-immunization, unfavorable placental implantation, etc., has statistically reduced their chances of producing normal children in the future. In some instances, this reduction will not be sufficient to warrant the physician's advising strongly against future pregnancies. With respect to the birth of a mongoloid child, it has been my experience that the chances are better for subsequent children to be normal when the parents are in their 20s than they are when the mother is in her late 30s or early 40s.

As mentioned previously, most mental deficiency apparently is the result of heredity. It is well known that when both parents are defective nearly all of the children (95 per cent) will be abnormal. If one parent is mentally defective and the other is normal, the children will be about evenly divided with respect to mental deficiency and normal potential. It is perhaps worth remembering that even when both parents are apparently normal there still exists a 1 to 3 per cent chance that deficiency may occur in the children of that couple. This is not meant to deny an equally well-known fact that some of the world's intellectual giants have unexpectedly come from apparently average parents. It seems that there are several "leavening" influences which tend to keep the population from becoming eventually divided into two groups, the one extremely brilliant, the other extremely retarded. It is well that this is so.

Questions and Answers

The following are questions commonly asked by parents, and the answers are based on views and opinions developed at various conferences and round-table discussions.

QUESTION: How can the physician best handle the problem presented by the birth of a mongoloid child?

ANSWER: Needless to say, the diagnosis of mongolism should be established before the parents are advised of this catastrophe. If necessary, consultation should be obtained; in fact, it is usually advisable to have more than one opinion if there is doubt about it. Bakwin has outlined a course of procedure which might well be a guide for physicians. He said that the parents should be told frankly and with as much kindness as possible about the true condition of their child. Certain offensive words like idiot, mongol, monster, etc. should be

avoided, since they will aggravate the hurt to the parents, and they do not mean the same thing to the layman that they do to the physician. It may be possible to ease the situation a little by pointing out that the mongoloid child is not deformed in the ordinary sense nor is he in any sense a monstrosity. He simply has signs and symptoms which inevitably point to a severe limitation of his ability to learn that which he must learn and to become independent and self-sufficient.

It is extremely important that parents be told that the etiology is not established and that there should be no feeling of guilt or the thought that the child's condition resulted from an overt action or thoughts of rejection which the parents might have had. At some time in the discussion, but possibly not at the first session, matters of heredity and the possibility of subsequent children being similarly afflicted must be brought up and discussed fully. Eventually, the subject of institutional care must be introduced, and it may well come up even at the first conference with the parents. As a rule, this subject needs to be approached very carefully with the idea that the family and physician are attempting to make proper provision for a child with mental handicap rather than with the idea that they are trying to get rid of a defective, unwanted child. Above all, the physician should impart to the parents his sympathetic and continued interest in their problem and their child, and the fact that he expects to advise them repeatedly until the problem is satisfactorily solved.

QUESTION: Admitting that eventual institutionalization is the best solution for the severely mentally retarded child as represented by the mongoloid, when should such a child be removed from the family to a custodial institution?

ANSWER: Not all physicians agree as to how this question should be answered. A generation ago, most pediatricians followed the thinking of Brenneman and many others who felt that such children should be separated from the family at the earliest possible moment, preferably taken from the lying-in hospital to an institution or to a boarding home pending admission to the institution. There has been some change in this view, and many pediatricians, psychiatrists and others feel that such precipitate action is harder on the mother of such a child than a course which permits the parents to take the child home and to keep him until they are able to understand the problem fully, and to accept by degrees the necessity for placing the child in a protected environment for his own good as well as the good of the other members of the family. This school of thought fears that the abrupt removal of the baby from the maternity hospital leaves the mother with the feeling that she produced something so defective and possibly monstrous that the doctors do not want her to see the child and, indeed, feel that it should be hurriedly removed to some place of relative concealment. Also, she may have some lingering doubt that the diagnosis was correct.

There is nothing repulsive about the ordinary mongoloid child, and, in most instances, the parents can take him home and take care of him until such time as they can fully accept the physician's recommendation that the world will not be receptive of him and is more likely to appear to him to be cold and rejecting, and that he will be better off and happier in the institutionalized environment where he can be with children like himself and where the tempo is suited to his capabilities and he is understood rather than pitied, scorned and rejected. There is one practical consideration—it is not possible to place all mentally defective children in institutions. There just are not enough beds for them.

Attention should be paid to the observations set forth by the professorial staff of the state home and training school institutions to the effect that the mongoloid or mentally defective child who can stay with his own family until he is four or five years of age is usually in somewhat better mental and physical condition than the child who comes to the institution in infancy. Florence Stewart, Director of the Lockland School, Geneva, New York, has still another reason why the family may, in the long run, feel better about their child if they have not rushed him out of the home. She said, "My experience has convinced me that parents who keep such a child at home

as a loved member of the family until he is three or four years of age are better able to accept his handicap and relinquish the later care with less pain because they have the satisfaction of having given several years of tender care. . . ."

QUESTION: What about the child with spina bifida and myelomeningocele?

ANSWER: Many children with this common combination of anomalies are normal mentally and will remain so if they escape complicating hydrocephalus. When the child has a gross anomaly such as to render him shocking and possibly repulsive to his mother, the problem of what to do is further complicated. When the deformity is gross and of such character as to be incompatible with successful surgical or other treatment, the situation calls for removal of such a child from the family, usually without the mother having seen the child. There certainly is no way to obviate severe mental trauma to the parents in such instances, but, with the exception of an unusually mentally stable mother, such infants should not be taken home. Large myelomeningoceles or teratomatous growths must indeed strike horror and terror into a mother's heart. The problem is not so simple when the infant with a myelomeningocele appears to move his lower extremities and hydrocephalus has not developed or may not do so. In this instance, it is desirable to have the mother care for the infant unless the physician believes she is not up to it. A few such children do escape hydrocephalus, and the meningocele sac may be removed at a later date.

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More than half the gynecic complaints heard in office practice are largely functional. The author advises that the psychiatric specialist should treat the more complex psychoses, but suggests that the general practitioner or gynecologist can and should manage functional disturbances of menstruation, pelvic pain in the absence of major objective gynecic pathology, leukorrhea, sterility and frigidity. He also reviews various therapeutic measures which may be applied.

Psychosomatic Office Gynecology

JEROME S. MENAKER

Wichita, Kansas

JEROME S. MENAKER

THE practice of medicine has changed dramatically in the score or so years since Flanders Dunbar first coined and popularized the word "psychosomatic." Giant strides in such fields as chemotherapy, antibiotics, surgery and endocrinology have made it difficult merely to keep abreast of the most significant advances. Unchanged, however, is the fact that in every patient are the two components of the psyche and the soma. It is our awareness of this omnipresent dual structure in every clinical disease process which has undergone phenomenal change.

Each of us who treats female patients, as general practitioner or specialist, has the responsibility of weighing the functional component in organic conditions and the organic component in functional complaints. No one has greater need and opportunity for evaluating psychosomatic complaints than the physician who treats gynecologic patients. The most conservative authors class as largely functional above 50 per cent of the gynecic complaints heard in office practice. If this classification were amenable to statistical scrutiny, a more accurate figure would be about 80 per cent, although enthusiasts for the psychodynamic approach would place the figure even higher.

Since diagnosis and treatment of psychosomatic gynecologic problems loom so large in the practices of all who treat women, it seems in order to review the more frequent problems encountered in this area. The psychosomatic problems of obstetrics deserve a full consideration separately and are not discussed here. An attempt will be made to integrate the psychodynamic approach and our special knowledge of female disorders within the normal frame of reference. The more complex problems of psychosis and of severe psychoneurosis are best handled by the psychiatric specialist. The conditions considered here can and should be managed by the trained and oriented general practitioner or gynecologist. These common conditions are: functional disturbances of menstruation, pelvic pain in the absence of major objective gynecic pathology, leukorrhea, sterility and frigidity.

Dysmenorrhea

Primary dysmenorrhea is a functional disturbance of uncertain etiology. Many conflicting and unproved theories place the basis of the difficulty in the uterine musculature, the

vascular system or the endocrine system. In spite of these contradictions, it is widely recognized that primary dysmenorrhea is much more frequent in the "high-strung, nervous or neurotic" woman. The emotional significance of menstruation to most women helps explain the psychic basis of dysmenorrhea. The wealth of literature on this subject includes a review by Chadwick of the taboos to which the menstruating woman has been subjected in ancient and even in modern and presumably more enlightened times. If one can believe the language of women, menstruation is not only a badge but the curse of femininity. Indeed, "the curse" is a term often applied to the menses. Brush has listed many other colloquialisms by which menstruation is known, most of them alluding to a state of ill health.

The very extrusion of blood itself is considered by many women to be evidence of illness, injury and unpleasantness. Envy of the masculine and rejection of the feminine role make up one of the better-documented tenets of analytic psychology. To many women, menstruation is a monthly subconscious reminder of inferiority. The secrecy and distaste with which most mothers discuss the subject with their daughters do little to dispel feelings of inferiority and resentment, which often begin at the menarche.

That primary or idiopathic dysmenorrhea can often be cured by simple suggestion seems beyond dispute. The fact that the condition can also be relieved by hormones, presacral neurectomy or other means is not contradictory. Psychologic factors act on the body through the media of physiologic change, for example, the blush and the tear. The literature contains numerous reports of excellent results from the psychosomatic approach to dysmenorrhea. Novak and associates have furnished evidence of such therapeutic success, often with brief and superficial psychotherapy.

The case of a young student nurse who had had severe dysmenorrhea since menarche affords an example of the relief often provided merely by explanation and reassurance. The patient's mother had died in childbirth, a fact impressed on her as early as she could remember. She had been raised by an irascible, bitter maiden aunt, who herself suffered volubly from dysmenorrhea. As a child, the patient had been made to stay home from school during each of her periods. She experienced not only cramps, but also a kind of enforced invalidism. As a student nurse, she had been unsuccessfully treated with antispasmodics, sedatives and anodynes. Three explanations of the physiologic aspects of menstruation, the production of two pain-free periods by the interruption of ovulation after the method of Ingersol[1] and the establishment of insight have largely relieved the dysmenorrhea. The patient never misses duty during menses and needs only simple anodynes for complete comfort.

This case is an example of excellent results quickly obtained in the relief of a frequent and often disabling complaint which is a daily challenge in our practices. The coordinated approach to primary dysmenorrhea is available to all of us, but Kroger and Freed[2] have warned that the general practitioner and the gynecologist may be confused by these patients if they expect to find surface evidence of emotional problems. Except during menses these patients often present a façade of poise and maturity which conceals underlying emotional instability.

Amenorrhea

Amenorrhea is another functional disorder of the menstrual cycle often caused by emotional disturbances. It is frequently seen in patients who have either an intense desire for pregnancy or a great fear of conceiving. In fact, psychogenic amenorrhea due to the fear of pregnancy has led women to the criminal abortionist, although no pregnancy existed. It is believed that separation is a frequent stress factor in psychogenic amenorrhea. This has often been demonstrated in servicemen's wives in wartime. Heiman,[3] however, emphasized separation as a specific etiologic factor in excessive functional uterine bleeding. That separation can also be a factor in amenorrhea has been documented too often to be denied.

Kroger and Freed[2] stated that loss of a loved one, especially the father, may precipitate amenorrhea. Among other factors to be considered they mentioned shock or accident,

emotional tension provoked by argument, radical change of environment or occupation, sexual maladjustments, psychosis and drug addiction. I have often noted psychogenic amenorrhea in student nurses at the time of state board examinations.

In my experience fear of pregnancy is the most frequent of the many psychic factors that can precipitate amenorrhea. A typical case was that of a 24 year old patient who had two children under the age of one. After a single postpartum menstrual period, her expected menses were overdue and she became frantic. She feared that either the rhythm system of contraception or her own mathematics had failed her. On being shown a slide of her own cervical mucus, which beautifully illustrated the "fern leaf" pattern, and being reassured that this meant she was not pregnant, she felt relieved. Within 20 minutes after leaving the office she began to menstruate. In this example, the rapidity of response would preclude a change in hormonal control via the emotions, so one must conclude that control of menstruation can also be mediated by direct neurogenic effect on endometrial vascularity.

Menometrorrhagia

Hypermenorrhea and polymenorrhea are frequently caused by emotional imbalance, but their psychogenic origin often is not recognized. Such abnormal bleeding is frequently seen in psychotics and often spontaneously ceases after amelioration of mental symptoms under therapy. While a role has been postulated for the hypothalamus, the underlying aberration seems to be in the pituitary-ovarian cycle. No one personality type seems to be consistently associated with menometrorrhagia. The disturbance, when not objectively organic, usually reflects an intense personal conflict. Such a conflict was hidden in a young single girl who had menometrorrhagia intractable to three curettages and the gamut of hormone therapy. Attention to psychic influences brought to light a turmoil over repeated incestuous advances by her father. She was torn between what she felt was morally right and a sense of filial respect or love, engendered by religious training. Her subconscious defense was to menstruate all the time. Once rapport was established and the diagnosis made, the patient left home, joined the WAVES, subsequently married, and now has one child. At no time has she had further excessive uterine bleeding.

The psychosomatic approach has, of course, limitations. When he feels it advisable to refer a case, the gynecologist should not forget that the psychiatrist may diagnose the existence of a problem without being able to discover what the problem is, much less resolve it. Menninger has described the case of a woman who menstruated every time her husband came home on leave from the Air Force, no matter how carefully these visits were timed to avoid such an occurrence. The couple appeared to love each other, and even psychiatric consultation did not disclose any conflict.

Vaginitis and Leukorrhea

Vaginitis and the resulting leukorrhea have long been classified in three types, depending on the etiologic agent responsible. The treatment has traditionally been an assault on the offending microorganism. Recently a new villain, the ultrafastidious *Hemophilus vaginalis*, has been nominated. The recurrence of these conditions, their persistence, and their resistance to the most enthusiastic therapy are impressive. The Menningers long ago pointed out the association of leukorrhea and emotional conflict; more recently, Moore and Simpson convincingly stressed this connection.

One patient had been treated unsuccessfully by 17 physicians with a like number of remedies for a severe trichomonal vaginitis. Finally, the patient herself realized that her worst attacks were invariably precipitated by her husband's alcoholic sprees. The couple sought counseling, after which the husband joined Alcoholics Anonymous and the wife's vaginitis disappeared. She was free of symptomatic trichomonal infestation until the death of her mother, at which time a vaginitis responded promptly to mild local therapy and mild sedation. As in this case, it is often the patient herself who achieves insight enough to point out to the physician the cause-and-effect association between "nervousness" and

exacerbations of organic complaints. Nowhere have we found this more true than in recurrent cases of vaginitis, yet many physicians are still reticent to accept this association.

Infertility

That fertility may be significantly affected by psychologic factors is knowledge as common to the layman as to the gynecologist. The popular reports of childless couples who conceive shortly after adopting a child, or often after only deciding to adopt, are no doubt exaggerated. The number of scientifically recorded cases is relatively few. Orr reviewed the subject in 1941, and carefully recorded analytic studies of a couple who conceived shortly after the decision to adopt. Workers have advanced various theories to explain the exact mechanism of this unexplained phenomenon. Dramatic physiologic change obviously is mediated by the emotions through the nervous and endocrine systems. I have known several couples to conceive only after abandoning infertility studies, and it may be that the eagerness and the emotionalism involved in these studies may help defeat their very purpose. Overzealous use of the basal temperature chart may prevent as many pregnancies as it assists.

Stone has recently reported an encouraging analysis of the Margaret Sanger Research Bureau's successful work with 500 cases of infertility in which emotional factors were seen as the largest single cause of childlessness. Psychologic tensions were believed to be primarily responsible for preventing 122 of the couples from becoming parents. Only five of these couples, however, needed intensive psychotherapy to help achieve the desired pregnancy. Our experience indicates that no study of the infertile couple can be considered complete without careful consideration of emotional as well as organic factors.

Frigidity and Dyspareunia

The medical profession, at least, generally agrees that bilateral sexual gratification is the norm in married couples. That the majority of married American women do not achieve this norm or ideal is also widely accepted. Psychiatrists themselves, not to mention gynecologists, are in such disagreement on precise definition of frigidity, and even orgasm, that full amplification of this subject belongs to more extensive works. The rare incidence of true constitutional frigidity, based on actual relevant organic pathology, suggests that in the "frigid" patient, the gynecologist must look for emotional factors or refer the patient to someone who will. He can do much to help the patient who complains that she does not "get much out of intercourse" or who "would rather he didn't touch me." That this is a frequent problem there can be no doubt. I remember the remark of a well-trained colleague who said, after a few months in private practice, "I had no idea there were so many women who couldn't stand to have their husbands touch them."

Diagnosis is simple. Given the chance, women are often willing to tell the physician of their lack of responsiveness, absence of climax, or even repulsion for sexual intercourse. In many cases deep-seated frigidity should be referred to the psychiatrist, but no less an authority than Mandy[4] has said, "As often as not the private practitioner can help these patients as much as the psychiatrist." In severe cases the problem may be so deep-seated that even prolonged analysis will not bring about a cure. The patient who can be greatly helped is often the one who has no insight even when the difficulties are most obvious, or to whom counseling can open up new and healthier attitudes to sex in marriage. A simple explanation of what is normal in sex has helped many grateful patients. For example, I have seen a number of patients who thought their husbands were hopeless perverts because they suggested cunnilinction. While I do not share Van de Velde's[5] romanticism about the "genital kiss," I have seen many patients greatly relieved to learn that it is not abnormal.

Kroger and Freed[2] made an excellent case for the prophylaxis of dyspareunia and frigidity. I believe that the best results will show up in the children of the patients we counsel in psychosexual problems. By redirecting the patients' attitudes we can prevent much injurious conditioning in their children. One cannot be-

gin to calculate the sexual ignorance and unhappiness that was spawned in the overstrict and puritanical homes of a generation or two ago. Frigidity and dyspareunia are not distinct clinical entities, but symptoms of emotional disturbances begun during early psychosexual development.

Therapy

Discussion of therapy should be prefaced with a reminder that we are considering psychosomatic complaints within the normal range of variation. The psychotic and the severe psychoneurotic should be referred to a psychiatrist. The therapeutic measures considered here are those which the oriented physician can and should apply. His approach should integrate interest, special knowledge, an understanding of simple psychotherapeutics, and common sense. He must first be interested and unhurried. The emotionally disturbed patient is quick to sense impatience, and this will deter her from talking out her problems. This talking takes time, but when guided by an interested physician it can have powerful therapeutic value. Often the patient needs only the opportunity to present her case. The physician must maintain a sympathetic and permissive attitude; either a sentimental or a critical attitude will destroy rapport. The physician's interested listening should give him insight into the patient and her problems. Often one carefully phrased question can induce the patient to ventilate much relevant material. By skillful management of the conversation, the physician can also begin to develop the patient's insight into her problems.

The patient requires a complete and careful physical examination with indicated laboratory work, for several reasons. The diagnosis of emotional illness is not a diagnosis of exclusion. If organic disease is present, its presence and extent should be determined; the patient will be reassured and will place greater confidence in the physician.

While the psychotherapeutics of education, explanation and reorientation are being carried out, the therapist is justified in employing drugs to alleviate symptoms and to make the patient more amenable to therapy. I usually prescribe DEXAMYL®, for mood amelioration and relief of the gloom and tension often seen in these patients, and various atractic drugs. Of the latter, the meprobamates are most often used. Therapeutically effective doses of these drugs may be used singly for either effect or in combination to relieve tension and promote a sense of well-being. The patient thus receives symptomatic relief while undergoing treatment designed to bring about more lasting results. The physician must exercise discretion in the use of these drugs; the patient's expectations should be realistic from the outset. The doctor should carefully explain that the drugs are symptomatic treatment, not a cure for psychosomatic illness, and that real relief will be achieved as emotional problems are resolved.

The cardinal fact is that the management of most psychosomatic gynecologic problems is not mysterious or esoteric. We can and should diagnose and treat most of these disorders in a relatively brief time by applying knowledge and skill already in our armamentarium. What is needed is neither a brush-off with the statement that "it is all in your head" nor immediate referral to a psychiatrist, but attention to the time-honored modalities of medicine, diagnosis and treatment—a complete examination and careful history taking. The physician also must take the time and interest to explain to the patient. On the surface it may seem that such a program is too time-consuming for a busy practitioner. In truth, time will be saved and high rewards gained in improved health for the patient and satisfaction for the physician.

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Scientific Exhibit

Drug Evaluation in Rheumatoid Arthritis

A Comparative Study of

Aspirin
Phenylbutazone
Cortisone
Prednisone

CHARLEY J. SMYTH, ROBERT L. JOHNSON AND GLENN M. CLARK*

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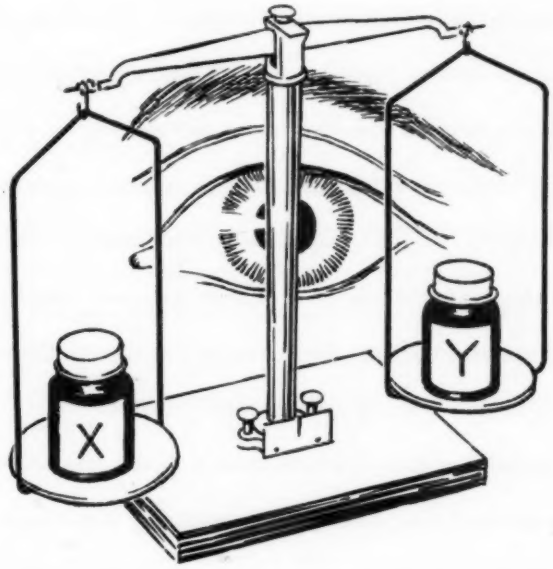

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Adapted from an exhibit shown at the 1958 annual meeting of the American Medical Association.

Introduction

EVALUATING any new drug for treating patients who have rheumatoid arthritis is extremely difficult. This becomes particularly evident in long-term studies in which an attempt is made to appraise the end results of specific therapy. Many experienced observers who have thoughtfully considered this problem doubt the reliability of current methods to measure the response of the disease to new agents. Recognizing the need for more objective and dependable methods for evaluating antarthritic drugs, the authors have made this study.

A quantitative method of evaluating response to therapy in patients who have rheumatoid arthritis by using the double-blind technic was designed to determine the value of phenylbutazone (BUTAZOLIDIN®), cortisone and prednisone as compared with aspirin. In a preliminary report in the June 1957 issue of the *Journal of Chronic Diseases*, this method was described and quantitative changes in the functional capacity and joint inflammation were expressed as numerical indexes. More extensive trials with this method revealed that it was unnecessarily complex and, furthermore, that some of the various functional tests gave unreliable data. A modification of the original method is emphasized here. Procedures for obtaining these simple measurements and results of the data acquired in a study of 32 patients who have rheumatoid arthritis are presented, and suggestions for further refinements in the method are discussed.

Components of an Evaluation Program

Selection of patients

Patients were chosen at random from those attending the Arthritis Clinic at Colorado General Hospital, and the diagnosis was conclusively established.

Excluded were patients having rheumatoid arthritis for less than one year and those with cardiac failure, renal disease, anemia or a history of peptic ulcer.

Double-blind technic

- All medications are code-labeled.
- All medications appear identical.
- Patient is unaware of change of medication.
- Physician is unaware of identity of medication.
- Dosage adjustment is allowed within limits.
- Aspirin or placebo, or both, are included for control.
- Sequence of drug courses is interposed with placebo or aspirin.

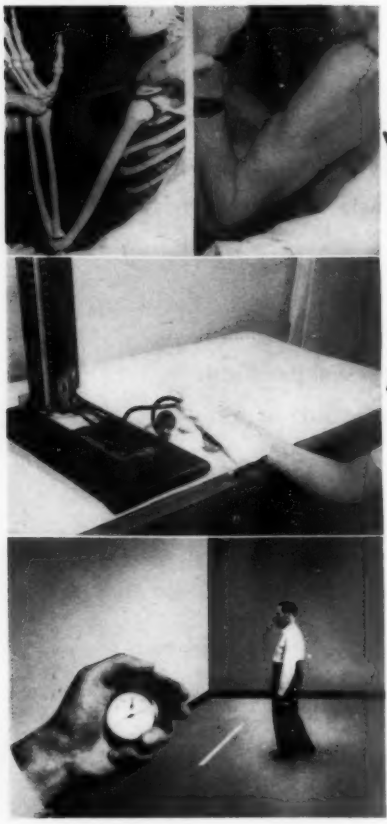
Plan of study

Aspirin was administered one month before and after each test drug.

Test drug was administered for five months.

Patients were examined before and after each test drug series.

Measurement of functional capacity



Reliable

1. Styloid-acromioclavicular distance in centimeters
2. Grip strength in millimeters of mercury, using sphygmomanometer cuff
3. Time in seconds to walk 25 ft.

Unreliable

1. Finger-tip apposition
2. Ability to make a fist
3. Heel-ischial tuberosity distance
4. Sitting normally

Measurement of inflammatory activity

A standard method was used to record degree of joint inflammation on an arbitrary scale of plus values ranging from one to four. The sum of these plus values for all joints showing active inflammation at each original and re-evaluation examination reflects the amount of total inflammation and can be expressed as a numerical value.

Reliable indicators of inflammation

Test for pain on motion in hip joint

Swelling of interphalangeal joints measured by ring size

Palpation for presence of fluid in knee joint

Heat

Redness

Tenderness

Unreliable indicators of inflammation

Erythrocyte sedimentation rate (Westergren method)

Sheep red blood cell agglutination test (Ziff modification)

Relating the degree and amount of inflammation to the percentage of total joint surface involved does not increase the reliability of the data, and unduly complicates the method.

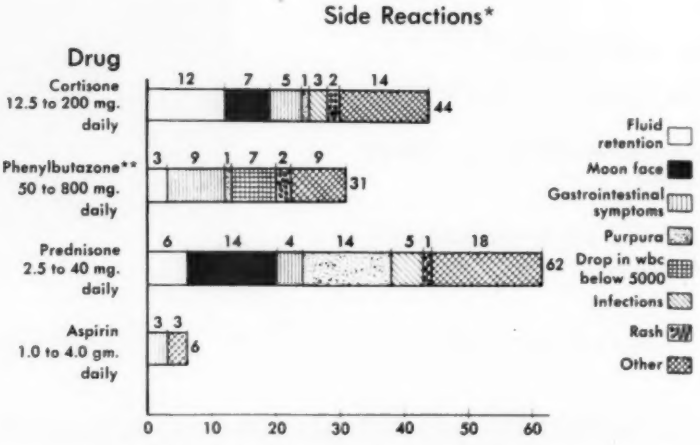
Roentgenographic changes

Roentgenograms of small joints of the hands, wrists and feet proved most valuable for detecting progressive involvement of cartilage and bone.

The five month test period on each drug was too short to reflect any consistent changes in the roentgenograms; therefore, individual films were made at six month intervals, and were read separately by three observers.

Recording of toxic reactions

Undesirable reactions, including fluid retention, moon face, gastrointestinal symptoms, purpura, infections, rash, a drop in leukocyte count below 5000 cells per cubic millimeter, and other side effects were noted.



*Tabulated on the first 25 patients who received one full course of each drug.

**Gastrointestinal symptoms necessitated discontinuation of drug in four patients.

1. Careful verbal and physical examination at each visit.
2. Weight, blood count and urine checked periodically.
3. Patients warned to report immediately any unusual symptoms.

Application of Methods in Drug Evaluation

In analyzing the end results of therapy with aspirin, cortisone, phenylbutazone and prednisone, no attempt was made to appraise such clinical subjective responses as pain, muscle spasm, weakness, anorexia, fatigue and lack of a sense of general well-being. Attention was concentrated on three selected factors which may be measured with considerable accuracy.

1. Changes in the functional capacity as manifested by the patient's ability to perform specific tests
2. Changes in the objective signs of inflammation
3. Structural changes as shown in serial roentgenograms of affected joints

Changes in functional capacity

TABLE 1

Mean Changes in Functional Capacity Measurements

Number of Patients	Drug Sequence	Functional Capacity Measurements		
		Grip *(mm. of Hg)*	Time to walk 25 ft. *(seconds)*	Styloid-acromioclavicular distance *(cm.)*
26	Aspirin Cortisone	+28.7	−0.78	−1.0
23	Cortisone Aspirin	−30.1	+0.71	+0.5
21	Aspirin Phenylbutazone	+31.3	−5.50	−2.0
26	Phenylbutazone Aspirin	− 6.8	−0.19	+0.4
13	Aspirin Prednisone	+61.9	−1.50	−1.1
18	Prednisone Aspirin	−30.8	+3.90	+2.8

Functional response

Results of functional capacity tests for each drug sequence were combined by a simpl ranking system and expressed as an index to show comparative response. This was nec essary since dimensions and magnitudes of change in each test were completely differen and it was desirable to express all changes on a common scale.

When changed from aspirin-to-cortisone (26 patients), the mean functional index associated with the change was +48.4 (+ implies increased function); from cortisone-to-aspirin (23 patients), the index was —45.8.

From aspirin-to-phenylbutazone (22 patients), the index was +47.4, while for the reverse sequence of these drugs (26 patients) the index was only —3.8.

The best response in functional index was noted with prednisone. The index was +66.0 for aspirin-to-prednisone (13 patients) and —59.3 for prednisone-to-aspirin (19 patients).

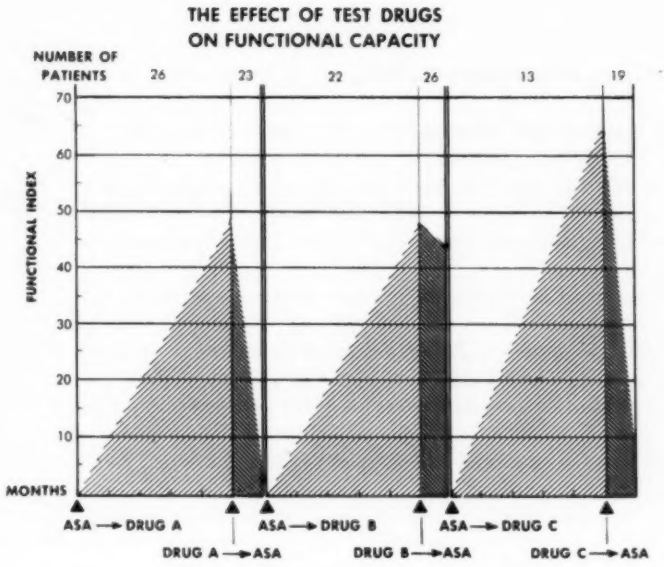
Anti-inflammatory response

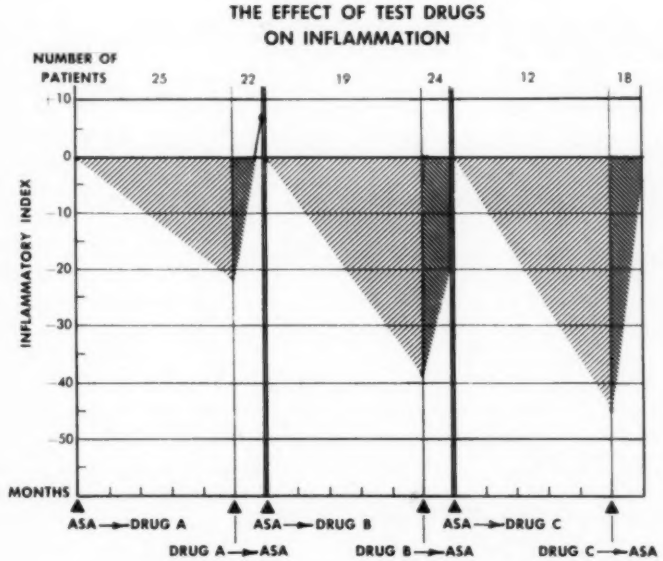
Changes manifesting alterations of objective clinical signs of inflammation were converted to numerical values and expressed at the end of each test period as an index of total inflammation. The mean value of these indexes was obtained for each group of patients in any particular drug sequence. The difference between the mean index calculated from aspirin control data and that calculated from the test drug data was expressed as a percentage change with aspirin data as a reference.

From aspirin-to-cortisone, the mean index changed —22 per cent (— implies decreased inflammation) (25 patients); from cortisone-to-aspirin, the opposite effect (+29 per cent; 22 patients) was observed.

From aspirin-to-phenylbutazone, the mean index changed —39 per cent (19 patients); for the reverse sequence, the change was +21 per cent (24 patients).

Prednisone after aspirin caused a —45 per cent (12 patients) change in the index, and an opposite change of +40 per cent (18 patients) when the drug sequence was reversed.





A = CORTISONE
12.5 to 200 mg. daily

B = PHENYLBUTAZONE
50 to 800 mg. daily

C = PREDNISONE
2.5 to 40 mg. daily

Summary

The index measurements shown reflect the influence of drug action in two directions for both function and inflammation. The choice of aspirin as a control drug may be open to question; however, the results suggest that it has a minimal effect compared with those of the other three drugs used in this study. The bidirectional evaluation of the test drugs is a stronger test than evaluation by a single sequence. In this regard, function increased and inflammation decreased during the administration of the test drug following aspirin; opposite effects were observed when aspirin followed the test drug. If the magnitude of response indicates the effectiveness of the test drug, prednisone becomes the most effective preparation, while cortisone and phenylbutazone are about equal. It is interesting that the phenylbutazone-to-aspirin sequence resulted in the minimal reverse response for both function and inflammation. More careful evaluation of these data indicates that phenylbutazone may have a more prolonged effect than either of the other drugs. Further refinements of this method are under investigation.

This study was made possible by a grant from Geigy Pharmaceuticals, Division of Geigy Chemical Corporation, Ardsley, New York.

Prednisone was supplied by Schering Corporation, Bloomfield, New Jersey.

Statistical analyses of data were made by Charles J. Hlad, Jr., Veterans Administration Hospital, Denver, Colorado.

Exercise and Weight Control

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In the preceding article in this series I attempted to give an over-all picture of the present knowledge of caloric requirements; various factors were enumerated which can be added together to determine how many calories a given patient should consume in order to maintain his body weight. I heavily emphasized the variability of that component of energy expenditure which has to do with physical activity. This range of variation of caloric expenditure due to exercise is of particular importance in the vexing problem of weight control.

In the past one or two decades, especially on this side of the Atlantic, the role of exercise in weight control has been minimized, if not ridiculed, by a number of lay health educators and sometimes (let us recognize it) by professional workers as well. The basis of this repeated denial has not been experimental work or clinical observations. Nor has it been the weight of the accumulated experience of the centuries, which has always contrasted the lean, hard, active soldier or hunter with the fat, sedentary merchant or clerk. Disparagement of the role of exercise in weight control has been based on two plausible misconceptions. These erroneous beliefs are usually expressed in the two following statements: (1) Exercise requires relatively little caloric expenditure and, therefore, increased physical activity hardly changes the caloric balance; and (2) an increase in physical activity is always automatically followed by an increase in appetite and food intake and may, therefore, actually impair the success of a weight reduction program. Let us examine these two propositions in detail.

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Caloric Expenditure in Exercise

The first misconception, minimizing the caloric expenditure due to physical activity, should be avoided by anyone who has ever looked at a table of energy expenditure. Such tables illustrate the fact that the cost of expenditure can be high. Similarly, the National Research Council table of recommended dietary allowances for men gives a range of 2400

to 4500 calories per day, depending on the level of activity. The figure of 4500 calories per day does not represent an upper limit: Laborers, soldiers in the field, and athletes may require more than 6000 calories per day.

One frequently hears or reads such contrasting statements as the following: The caloric equivalent of 1 lb. fat can be matched only by walking for 36 hours, splitting wood for seven hours, or playing volleyball for 11 hours. These unattainable extremes of physical activity are used to demonstrate that it is impossible to lose weight by exercise. The implicit postulate is that the cost of exercise depends completely on its being done at one stretch. Actually, of course, the cost of splitting wood for seven hours is equivalent to 1 lb. fat, even though the seven hours may not be consecutive. Although splitting wood for seven consecutive hours would be difficult for anyone other than a Paul Bunyan, splitting wood for one-half hour every day is by no means an impossible task for a healthy man, and this would add up to seven hours in a fortnight. If it represented a regular practice, it would, by the very reasoning of the detractors of exercise, be the caloric equivalent of 26 lb. body fat in a year. A half-hour of handball or squash a day would be equivalent to 16 lb. a year.

It seems more useful, however, simply to recall the measured costs of different types of physical exercise. Table 1, modified and summarized from the work of Orr and Leitch[1] and from Passmore and Durnin,[2] gives approxi-

TABLE 1

CALORIE REQUIREMENTS FOR VARIOUS ACTIVITIES*

ACTIVITIES	CALORIES PER HOUR	ACTIVITIES	CALORIES PER HOUR
Domestic occupations		Running	800-1000
Sewing	10-30	Cycling	
Writing	20	5 mph	250
Sitting at rest	15	10 mph	450
Standing relaxed	20	14 mph	700
Dressing and undressing	30-40	Horseback riding	
Ironing (with 5 lb. iron)	60	Walking	150
Dishwashing	60	Trotting	500
Sweeping or dusting	80-130	Galloping	600
Polishing	150-200	Dancing	200-400
Industrial occupations		Gymnastics	200-500
Tailoring	50-100	Golfing	300
Shoemaking	80-100	Playing tennis	400-500
Bookbinding	75-100	Playing soccer	550
Locksmithing	150-200	Canoeing	
House painting	150-200	2.5 mph	180
Carpentering	150-200	4.0 mph	420
Joinering	200	Sculling	
Cartwrighting	200	50 strokes per minute	420
Smithing (light work)	250-300	97 strokes per minute	670
Smithing (heavy work)	300-400	Rowing (peak effort)	1200
Riveting	300	Swimming	
Coal mining (avg. for shift)	200-400	Breast and back stroke	300-650
Stone masoning	300-400	Crawl	700-900
Sawing wood	400-600	Playing squash	600-700
Physical exercise		Climbing	700-900
Walking		Skiing	600-700
2 mph	200	Skating (fast)	300-700
3 mph	270	Wrestling	900-1000
4 mph	350		

Figures obtained for 150 lb. subject. To be added to B.M.R. plus 10 per cent for specific dynamic action.

*Modified from Orr and Leitch[1] and from Passmore and Durnin.[2]

mate requirements per hour of exercise over basal rate, established for young men of average size (145 to 170 lb.).

It will be seen from table 1 that for the average man examples of energy expenditure over the cost of sitting (which is about 15 calories an hour over lying at rest) are: walking, about 250 calories per hour; swimming, up to 900 calories; cycling, up to 700 calories. These hourly rates of energy expenditure above the sitting level do not include the admittedly short-duration peaks of activity reached in competition, which may be as high as 1500 calories per hour. (A Scandinavian journal recently published a study showing that athletes expend between 4000 and 5000 calories during three hours of cross-country skiing!) An expenditure of 500 to 600 calories per hour above the resting level represents a rate of physical activity which the average middle-aged adult not in training can endure for a period of 30 minutes without undue discomfort. A healthy young adult, even if untrained, can, of course, tolerate such rates of expenditure for much longer periods. A few years ago, in an experiment conducted in the nutrition department at Harvard, undergraduates were made to double their food intake, already in the vicinity of 3000 calories, without increasing their weight. These boys had to work hard to achieve this result, especially since classes limited the time during which they could exercise, but they did manage to "lose" an extra 3000 calories per day.

The only heavy object moved in most types of exercise is the entire body or parts of it. Therefore, the energy cost of exercise is proportional to body weight. If excess body weight is so great that it impairs body movement, this relationship will no longer strictly apply, and the cost of exercise will actually increase faster than will body weight.

If the energy cost of exercise is approximately proportional to body weight, it follows that the overweight person will require more energy and hence burn more body reserves for the same amount of exercise than will a slimmer person. If a person is 20 per cent overweight, it will increase the cost of walking, tennis playing, golfing and such by 20 per cent. This represents a much greater proportional increase than that introduced by the increase in basal metabolism due to excess weight, which is proportional only to a fractional power of the body weight.

Thus, any increase of the caloric intake above balance level in a physically active person will cause only a modest increase in weight because of the energy cost of moving the extra poundage. On the other hand, a sedentary person will expend less energy in moving the extra weight; hence, weight gain will be more rapid and more pronounced. Therefore, a sedentary person will be exposed to the danger of overweight to a much greater extent than will a person who makes a practice of daily or, at least, frequent physical exercise.

Data from studies of experimental obesity support these concepts. In the hereditary obese-hyperglycemic syndrome of mice, a recessive form of obesity extensively studied in my laboratory, more than half the extra calories available for fat synthesis comes from inactivity rather than from hyperphagia. Measurement of the spontaneous activity of nonfasted animals in activity cages shows that obese animals are 50 to 100 times less active than nonobese animals. This inactivity is not the result of extreme obesity but, in fact, precedes it, as is shown by comparing the activity rates of mature nonobese animals with those of young obese animals of the same weight. It can thus be considered as one of the etiologic factors in the syndrome determined by the obese-hyperglycemic gene. Nonobese animals maintained at a constant weight consume about 20 calories per day, of which 10 cover basal expenditure and two cover specific dynamic action, leaving eight for the cost of activity. Obese littermates consume about 25 calories per day and may gain up to 1 gm. (nine calories) daily. Their basal is, again, about 10 calories per day, with specific dynamic action two and one-half calories per day. When the eight calories expended daily on activity by the nonobese mouse are ascribed to fat synthesis in the obese mouse, the rapid development of extreme adiposity is no longer a thermodynamic impossibility.

The weight gain of genetically obese mice

can be drastically reduced by treadmill exercise. The obese members of the strain who carry the "waltzing" gene and are in constant rotary movement in their cages show a weight gain only about 30 per cent greater than that of nonobese mice, instead of the 200 or 300 per cent shown by sedentary obese mice.

There are, as will be described in another article in this series, many forms of experimental obesities. (These various conditions may be models for a similar variety of human obesities.) The obese-hyperglycemic syndrome is a metabolic (endocrine form) obesity probably due to primary hypertrophy of the islands of Langerhans, with resulting hypersecretion of insulin and of the pancreatic hyperglycemic-glycogenolytic factor (glucagon).

Among the six or seven other forms of mouse obesity which have been described in my laboratory is hypothalamic obesity. This can be achieved by specifically destroying the ventromedial area of the hypothalamus by surgical electrocoagulation or, more conveniently, by the single injection of the chemical gold thioglucose. Mice in which hypothalamic obesity is produced by gold thioglucose differ from those with the hereditary obese-hyperglycemic syndrome in that they are normally active and use all the extra calories which they consume (up to 50 per cent above normal). Yet these animals will still lose weight if exercised on the treadmill or if given the opportunity to exercise in a squirrel-type rotary cage.

Such findings emphasize both the diversity of obesities in regard to spontaneous activities and the importance of exercise as a weight control factor.

Increased Food Intake in Exercise

A second frequent misconception concerning the value of exercise in weight control is that an increase in physical activity *always* causes an increase in appetite and food intake which equals or is greater in energy value than that of the energy cost of the exercise.

It is true that in a normal, reasonably exercised animal or person an increase in food intake follows an increase in activity. This explains why the weight of most adult animals and men is relatively constant. Proper adjustments of appetite prevent the body from indefinitely burning away reserves if the person is called on to perform at higher levels of exertion than previously customary. However, experimental results show that this is true only within a certain range, which I call "normal activity range." When the activity of rabbits is restricted by confinement in a small cage, they will consume more calories than they require and thus accumulate fat. The excess food consumed is characteristic of the strain; hence, a hereditary factor is involved. The same phenomenon is illustrated by the fact that rats become obese if they are totally immobilized.

The dependence of food intake and body weight on physical activity has been systematically explored in experimental animals in my laboratory. When mature rats, accustomed to a sedentary (caged) existence, were exercised on a treadmill for increasing daily periods, moderate exercise of short duration (20 minutes to one hour) did not result in a corresponding increase in food intake. Actually, food intake decreased slightly but significantly. Body weight also decreased (sedentary range in figure 1). For longer periods of exercise (one to five or six hours), food intake increased linearly and weight was maintained (range of proportional response, a normal activity range in figure 1). As a result of very long periods of exercise, the animals lost weight, their food intake decreased, and their appearance deteriorated (exhaustion range in figure 1). Both the sedentary and the exhaustion ranges can thus be considered "nonresponsive" with respect to food intake, because in these ranges an increase in activity is not accompanied by a corresponding increase in food intake.

Obviously, the sedentary nonresponsive zone is of particular interest to the problem of obesity. It demonstrates that under abnormal environmental conditions which force partial immobilization or, at least, a sedentary life on the subject the limits below which food intake no longer decreases because of a decrease in activity are overtaken. Adiposity is the unavoidable result. This, of course, has been known empirically to farmers for centuries and explains the practice of cooping or pen-

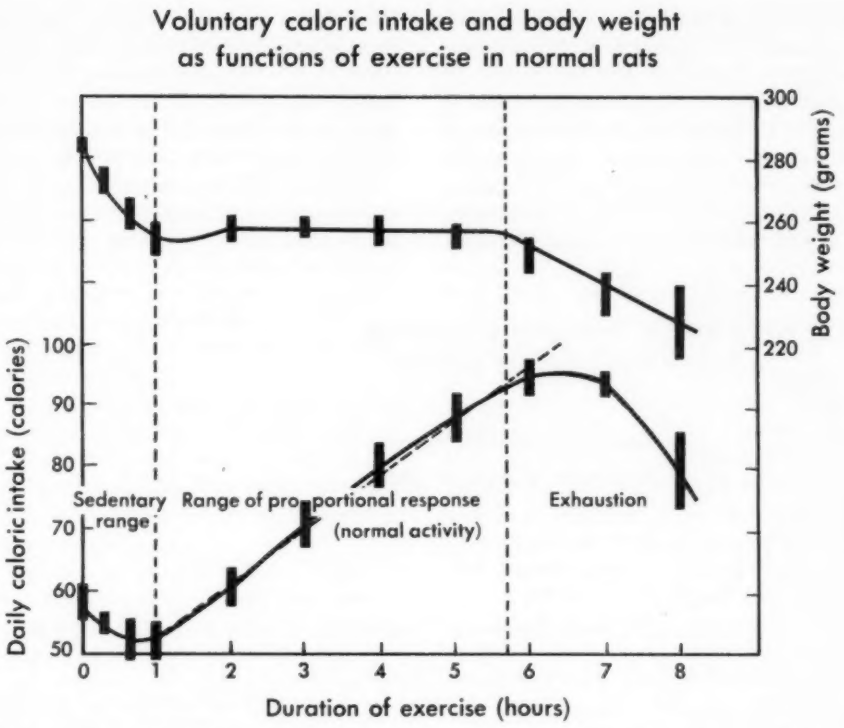

FIGURE 1. A summary of laboratory experiments, this graph shows that food intake does not necessarily increase with exercise in experimental animals. Although rats exercised for three or four hours daily eat more than those exercised for one hour, they maintain their body weight because of their activity. However, rats exercised for less than one hour daily or not at all eat significantly more, and weight accumulates because of the increased food intake and low activity level.

ning cattle, hogs and geese for fattening. Passmore confirmed these findings in a recent systematic study.

Similar observations are available concerning man. Greene studied more than 200 overweight adult patients in whom the beginning of obesity could be traced directly to a sudden decrease in activity. In the summer of 1954 I had an opportunity to conduct a study on an industrial population of West Bengal (India), which has a particularly wide range of physical activity, from bazaar tailors and clerks to coolies carrying twice their body weight on their heads for nine hours a day. Figure 2 illustrates the findings of that study.

The determination of food intake was facilitated by the fact that most of the persons surveyed did not live in a family situation, but bought their food and cooked for themselves. The lack of storage facilities forced them to shop frequently. The diet was extraordinarily uniform for each person and showed little variety within groups and from group to group. Individual one day dietary recalls, checked by buying records, and studies on amounts spent per week on food gave results generally identical with exhaustive dietary histories and appeared more representative of long-range intakes than did corresponding data obtained in a Western society.

Activity was determined by detailed schedules, industrial ratings of physical effort, and some Douglas bag determinations. Clerks were further subdivided into four classes, according to the mileage walked daily to and from work; those in class 1 were the most inactive, actual-

ly living within the factory grounds. The various occupations or subgroups were each represented by at least 10 persons and were grouped according to a broad classification of activity. One extreme included the merchants, supervisors and "nonwalking" clerks. At the other extreme were the selectors and pilers; carriers, who carried up to 190 lb. jute each; coalmen and ashmen, who carried equally heavy bags of coal and ashes and unloade them in an awkward manner; and cutters, wh spent their whole day swinging heavy cuttin knives with practically no pause. Individu weights varied from 67 to 198 lb. for men o the same height (5 ft. 2 in. to 5 ft. 4 in.).

Economic differences and cultural, religiou and ethnic factors could be accounted for an ruled out in analyzing the results. It is readil

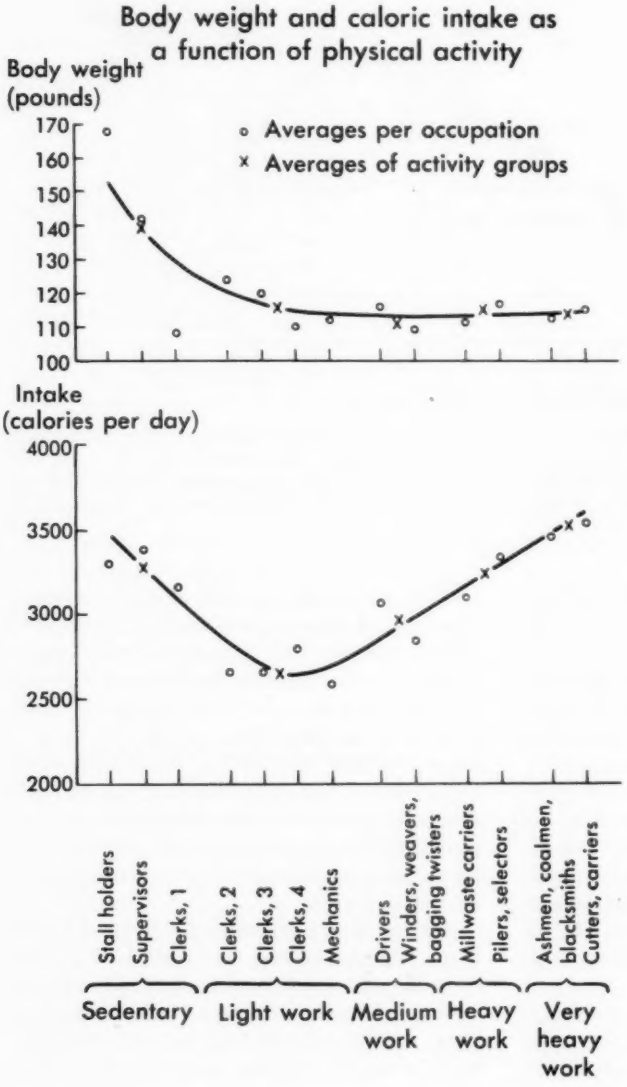

FIGURE 2. Results of a study conducted on a population in India, showing the relation of a wide range of activities to food intake and adiposity. Clerks are grouped according to the daily time spent in walking. As in experimental animals, persons who exercised regularly had the lowest daily food intake. Those who did heavy work ate more to maintain their weight. Inactive persons also ate more and became obese.

seen from figure 2 that the curves obtained for food intake and body weight as functions of physical activity are strikingly similar to those of figure 1, which were obtained on rats. Again, there is a sedentary range which corresponds to no further decrease in food intake (instead, to an increase) and in which increasing degrees of overweight follow decreasing exercise. Incidentally, the meaning of the actual increase in food intake under extremely sedentary conditions is not clear. It may indicate decreased ready availability of reserves, possibly resulting from circulatory sluggishness due to inactivity.

The work of Taylor and colleagues at the department of physiological hygiene, University of Minnesota, also showed that an increase in exercise above the very sedentary level was not accompanied by an increase in food intake in adult men.

The problem of the relation of weight to activity in children also has been investigated. Bruch found that inactivity was characteristic of the majority of the 160 obese children whom she studied. Only 18 per cent of the boys and 22 per cent of the girls were normally active. Seventy-six per cent of the boys and 88 per cent of the girls were physically inactive. Rony suggested that laziness or a decreased desire to engage in muscular activity is a primary characteristic of the obese subject; it is demonstrated in childhood by avoidance of all unnecessary activity, outdoor play and athletics. Bronstein found that most of the 35 obese children whom he and his associates observed spent most of their leisure time in sedentary activities. Graham reported like observations. Danish workers, particularly Tolstrup and Juel-Nielsen, attempted a semiobjective grading of groups of obese children and found that lack of activity was characteristic of these subjects. Peckos, studying a large group of Boston children, found that differences in body build and, more specifically, in fat content and distribution were not correlated with caloric intake. Fry determined that obese children with large fat pads did not have higher average caloric intakes than did control children of the same height and age. In her tabulation of "rough psychologic evaluation" a much higher proportion of obese children than of nonobese children are labeled as only moderately active or inactive. This difference was particularly marked in boys; however, no data were given to support this estimate.

In a recent study we attempted to compare systematically both caloric intake and activity in carefully paired groups of obese and normal-weight high school girls. Exhaustive research was conducted on dietary histories and activity schedules covering the year preceding the study. We correlated as accurately as possible the food intake of these teen-agers, with due regard for the difficulties encountered when applied to children and to obese subjects. Checks and counterchecks were conducted until we believed that reliable figures had been obtained. The picture of physical activity was determined by a system of successive examinations. A list of usual activities was established and the subjects were asked how much time they devoted to each on a daily or weekly basis, depending on the type of activity considered. The subjects were then asked to complete the list of activities and schedules, covering the year by seasons. Total hours per week were checked, and in another interview the activities were rechecked again on the same general basis. If the total time per week had been grossly overestimated or underestimated, special efforts were devoted to locating the cause of the error. The activities were rated on the basis of activity tables such as table 1.

We found that suburban high school girls were generally not very active; even the schedule of the nonobese group showed little time devoted to household chores, little participation in active sports, and, at least during the school term, a minimal amount of time devoted to walking or to other physical activity. Even so, there was a marked difference between the obese and nonobese groups. The obese group was much more inactive than the nonobese. Generally speaking, the time spent by the obese group in sports or any sort of exercise (including ballroom dancing) was less than half that spent by the thin girls, the difference being absorbed by "sitting" activi-

ties. (It may be worthwhile to mention that many of the obese girls and boys in the school system in which this study was conducted were all too often excused from the sports program by the educational authorities on the basis of a letter from the family physician recommending that they not be required to exercise!) By contrast, caloric intakes were generally larger in the nonobese than in the obese group. When possible, factors leading to positive energy balance were analyzed. It appeared that for this particular group, even when probable sources of error were recognized as inherent in the dietary interview method and in the type of activity analysis selected, inactivity was of greater importance than was overeating in the development of obesity. These high school girls, both obese and nonobese, attended summer camp each year; almost without exception the enforced strenuous activity caused loss of weight despite simultaneously increased food intake.

In another study a group of obese boys systematically exercised, and the evolution of their total body fat, measured by the determination of skinfold thickness, was followed. (Half the body fat is right under the skin and thus can be measured through the use of special calipers.) These boys did lose fat, and they presented a vastly improved appearance and mental outlook.

Comment

I am convinced that inactivity is the most important factor explaining the frequency of "creeping" overweight in modern Western societies. Natural selection, operating for hundreds of thousands of years, made men physically active and resourceful, well prepared to become hunters, fishermen or agriculturalists. The regulation of food intake was not designed to adapt to the highly mechanized sedentary conditions of modern life, just as animals were not created to be caged. Adapting to these conditions without developing obesity means either that the individual will have to step up his activity or that he will be mildly or acutely hungry all his life. The first solution is difficult, especially as present conditions in the United States—particularly in cities—offer little inducement to walking and often have poorly organized facilities for adult exercise. Even among the young, highly competitive sports for the few are emphasized at the expense of individual sports which all could learn and continue to enjoy after the high school and college years are over. But if stepping up activity is difficult, it is well to remember that the alternative (lifetime hunger) is so much more difficult that relying on it for weight control programs will only continue to lead to the fiascoes of the past. Strenuous exercise on an irregular basis is obviously not advocated for untrained obese persons. However, a reorganization of one's life to include regular exercise adapted to one's physical potentialities is a justified return to the wisdom of the ages.

If the responsibility of the family physician is not only to treat diseases but also to see that his patients achieve and maintain positive health and full realization of their physical possibilities, it becomes part of his task to see to it that this regular exercise, as well as proper food habits and sufficient rest, becomes an integral part of their daily schedule.

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Chronic Ulcerative Colitis

Medical Management

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Surgical Management

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Statement by Dr. Wakefield:

As soon as the diagnosis of chronic ulcerative colitis is established, it is well to tell the patient that the course of this disorder usually is characterized by relapses; and by comparison it is, to some extent, like rheumatic fever, rheumatoid arthritis and peptic ulcer. In answer to queries concerning complete recovery from chronic ulcerative colitis, it may be stated that doubtless recovery does occur. As in the other chronic disorders enumerated, however, there is no certainty that a relapse will not come, even after years of good health. Some persons have had one or more attacks of chronic ulcerative colitis varying in degrees of severity from mild proctosigmoiditis to the so-called fulminating instances of the disease, but have recovered with the colon so well healed that little objective evidence remains to indicate chronic ulcerative colitis ever had been present. In contrast, there are those whose ulcerative colitis has been stubbornly chronic, and this chronicity has caused profound structural changes in the colon which greatly hamper its functional capacity. During the first interviews, it is not good practice to dwell on the possible complications of chronic ulcerative colitis. If the patient comprehends the foregoing facts regarding the disease itself, the outline for treatment will be more significant.

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The routine plan of treatment for chronic ulcerative colitis embraces general hygienic measures. The diet should be high in proteins, vitamins and calories; and it should yield a low residue on digestion. In instances of obesity the type of diet remains the same but the caloric intake is reduced. Regular periods, preferably after meals, should be devoted to rest. In most cases they need not exceed half an hour. Infections of the upper part of the respiratory tract are especially prone to initiate a relapse; therefore, exposure to severe weather, chilling and getting wet should be avoided as much as possible. Patients with chronic ulcerative colitis should remain in bed as long as a cold with fever persists. Avoidance of excessive physical fatigue and emotional tensions is important. The plan for each patient should be adapted to his individual needs. It should embrace a routine for work and play and a wholesome attitude toward life both in relapses and in remissions.

In a great many instances of chronic ulcerative colitis, the foregoing outline of treatment will suffice to maintain a fair degree of health. In other cases the plan fails because neither the physician nor the patient has confidence in it. Also, failures ensue when the patient begins to indulge in unorthodox dietary measures and remedies. A trial-and-error plan of treatment, such as the use of every new drug that is offered for treatment of colitis, is sure to fail. Each time a drug or some other remedial measure fails to benefit the patient, confidence is lost, and the effective instillation of a sound plan of treatment is made more difficult.

The primary manifestations of chronic ulcerative colitis are: (1) an increased urgency to move the bowels; (2) lower abdominal discomforts and pain, and (3) the passage of blood and mucus in the bowel movements. Both the number of rectal discharges and the pain may have a daily periodicity, for instance, after breakfast. Along with the passage of blood and mucus in the stools, excessive fluids and electrolytes may be lost.

Management of Bowel Action and Pain

The tenesmus when mild may not require treatment; when severe, sitz baths taken twice daily may be of benefit, and opium tincture 5 drops in water, may be administered four times daily. The dosage of this drug should not exceed 10 drops four times daily. For the bedfast patient, hot wet applications may be applied to the perineal regions. Good nursing care may be required to prevent macerations of the skin in the regions exposed to the discharges. Often infected, swollen hemorrhoids and anal fissures develop during exacerbations. These conditions are treated conservatively and not surgically during the active phase of disease.

The pain in the lower abdomen, often crampy in nature, can vary from mild degrees relieved by bowel movement to severe cramping which may only partially be relieved by a rectal discharge. Often the cramping can be alleviated by the opium tincture administered as prescribed for the tenesmus. Use of opium tincture should not be continued longer than two to three weeks. In most severe instances of tenesmus it should be discontinued if the patient improves; and an antispasmodic, such as a mixture of belladonna tincture and phenobarbital elixir, should be substituted (8 to 10 drops of belladonna tincture to each dram of the phenobarbital elixir, 1 teaspoonful three times a day before meals until pharmacologic effects are obtained). In severe instances of chronic ulcerative colitis with fecal incontinence the tenesmus ceases, and the opium tincture no longer is of value. When fecal incontinence prevails, the patient should be diapered, using a diaper containing absorbent cellulose material. The diaper should be changed several times daily, the parts cleansed thoroughly, and the skin protected by some appropriate material, as for instance, zinc oxide ointment.

Maintenance of Fluids and Electrolytes

The rectal bleeding is not alleviated nor the colitis benefited by any known solid, liquid or gas placed in the rectum and colon by instillation, insufflation or irrigation. Likewise, astringent or bulk-forming materials (such as the tannins) given by mouth are of no value and may do injury to the bowel. Rectal bleeding manifested by anemia is treated by transfusions of 500 ml. of whole blood. The seri-

ously ill or critically ill patient should have frequent blood transfusions as a supportive measure even if no significant anemia is present. The fluid and electrolytes lost over each 24 hour period should be replaced by parenteral administrations of an isotonic solution of sodium chloride in distilled water. Replacement of lost potassium, which is necessary, can be done by adding 30 mEq. of potassium chloride to each 500 ml. increment of the isotonic saline solution until the required amount of potassium has been administered. The amount of all electrolytes administered should be controlled by determination of the electrolyte concentration in the blood. In fulminating forms of the disease, a fluid consisting of 7.0 gm. sodium chloride, 0.90 gm. potassium chloride, 0.34 gm. calcium chloride, and 0.28 gm. magnesium chloride in 1000 ml. triple-distilled water is a good one to administer to those patients who have a marked depletion of fluids and electrolytes.

Treatment for Secondary Infection

For the treatment of the secondary infection and thus the fever, various antibacterial agents are regularly administered to patients with chronic ulcerative colitis. These drugs may have definite beneficial effects. Perhaps the least harmful of them is salicylazosulfapyridine (azopyrin) administered in doses of 1 gm. every four hours around the clock. To ambulatory patients, 1 gm. is administered after meals and at bedtime for a period of two weeks, and this dosage may be repeated after three or four days of rest from use of the drug. To seriously or critically ill patients who have high fever (103° to 105° F.), potassium penicillin G, 200,000 to 600,000 units, may be given intramuscularly every six hours. It may be well to supplement the penicillin with streptomycin sulfate, 100 to 250 mg., given intramuscularly every 12 hours. When perforation, abscess formation or localized or generalized peritonitis is present, the treatment of these conditions requires intravenous administration of antibiotics such as chlortetracycline hydrochloride. There are various combinations of these antibacterial drugs which are satisfactorily employed.

Hormonal Medication

Cortisone and ACTH have been administered extensively as therapeutic agents in chronic ulcerative colitis with the hope that the great bodily depletions so prevalent during the severe exacerbations of the disease might be prevented or restored if these hormones were present. A few patients seemingly do respond as desired. Others have achieved remarkable temporary improvement only to lapse into complications of the disease, such as profuse hemorrhages, perforations of the intestines, or a psychosis which may be very difficult to treat. According to my experience, these hormones should be employed only with caution and, in fact, are not indicated by the disease per se in either its mild or its severe and fulminating forms. If such preparations are to be used at all, more benefit will be observed when they are directed against some complicating disorder of chronic ulcerative colitis—for instance, rheumatoid arthritis—or used only in selected cases of the disease. The patients chosen for the use of these hormones are those who have moderately severe ulcerative colitis in which the progress is not satisfactory and whose need for stimulation to create a better appetite and to attain a feeling of well-being is urgent. As soon as such beneficial results are obtained—if they are—a decrease in the dosage of the hormones should be instituted, leading to discontinuance. Without such results the trial should be limited to a few weeks.

Anorexia, Nausea and Vomiting

Frequently, loss of appetite, nausea and vomiting are severe. For the nausea and vomiting, a tranquilizing drug in an average dosage is often beneficial. Patients who have chronic ulcerative colitis complicated by nausea and vomiting do not tolerate well the so-called food concentrates, nor do they tolerate well tube feeding. During such periods in this illness, it often is best to offer and to permit small quantities of any food that may be desired if it can be tolerated. In periods of anorexia imposed by disease, transfusions of blood and parenteral administration of dex-

trose (5 or 10 per cent in an isotonic saline solution) are highly desirable supportive measures.

Scarring of the Colon

A complication resulting from the processes of healing may occur at any stage of the disease or during a remission. This is the formation of scar tissue which imparts a granular, irregular, pocketlike appearance to the mucosa. In the more severe instances of the disease, the mucosa and musculature are extensively replaced by fibrous tissue which, as it contracts, forms crevices and pseudopolyps. In themselves, pseudopolyps are of no great importance and may not require treatment; but they may be the site of carcinomatous changes at some time in the future. Along with the afore-mentioned scarring processes, fibrosis of the musculature causes thickening of the bowel wall with loss of elasticity and contractility and narrowing of the lumen. Stenosis and stricturing may occur in any segment of the colon, but it is most common in the rectum and rectosigmoid. The degree of stenosis and stricturing which may be present without manifest obstruction of the fecal stream is remarkable. At times the symptoms of intestinal obstruction ensue, however; and if the degree of severity is sufficient, surgical treatment becomes necessary. Stenosis and stricturing of the bowel in the presence of pseudopolypoid formations require close observation at intervals of three to six months because carcinoma develops more commonly in colons which are thus affected than in colons of those patients who do not have chronic ulcerative colitis.

Statement by Dr. Colcock:

ALL patients with ulcerative colitis should have a trial of medical treatment. However, many patients with this disease cannot be restored to normal health by medical treatment alone, and some will die unless an operation is performed. In any group of patients with ulcerative colitis, the number who require operation will vary according to the severity of the disease in that group. At present, 40 to 50 per cent of our patients with ulcerative colitis need surgery. This is required for one of two reasons: (1) to treat complications such as perforation, obstruction, hemorrhage or carcinoma, or (2) because of failure to respond to medical treatment.

BENTLEY P. COLCOCK

The acute fulminating form of ulcerative colitis develops in a few cases. These patients run a high fever, are extremely ill, and may die within a few days in spite of intensive medical treatment. Cortisone and ACTH will sometimes produce dramatic improvement, although they do not cure the disease. Nevertheless, prolonged steroid therapy is dangerous. The bowel wall becomes friable and adheres to surrounding structures. Spontaneous perforation may occur, and resection, if it becomes necessary, is hazardous. Therefore, if these patients fail to respond promptly to medical treatment, they should have an operation. Surgical intervention has saved the lives of many patients with acute fulminating ulcerative colitis.

Persistent, profuse rectal bleeding is uncommon in ulcerative colitis, but, when it does occur, operation must not be delayed too long. In the past, some of these patients have bled to death. Perforation is a common complication of ulcerative colitis and is always an indication for surgical intervention. Perforation often causes the development of fistulas between the colon and the vagina or bladder. These patients will require surgery. The ulcerative process in the colon leads to extensive fibrosis and narrowing of the lumen; and if obstruction occurs, surgery must be employed.

Carcinoma of the colon is a complication of long-standing ulcerative colitis. Five per cent of our patients with ulcerative colitis who come to surgery have carcinoma of the colon. The symptoms of cancer are frequently hidden by the abdominal pain, bleeding and diarrhea of ulcerative colitis. The carcinoma metastasizes early and the prognosis is poor. We

have been able to cure a few of these patients by early diagnosis and resection.

Most patients with ulcerative colitis come to surgery because they have failed to respond to medical treatment. If a patient begins to show clinical and roentgenologic evidence of chronic infectious arthritis, the ulcerated, infected colon should be removed. If this is not done, permanent crippling deformity may result. Certainly, surgery should be seriously considered for any patient who has been incapacitated for a long period of time. These patients are often unable to work or to stay in school because of malnutrition, chronic anemia or diarrhea (10 to 20 bowel movements per day). Some have been invalids for many months or years despite all forms of medical treatment. We know that surgical intervention can restore these patients to health and to normal social and economic activity.

For most cases of ulcerative colitis, surgical treatment is an ileostomy and colectomy, plus removal of the rectum. A few patients with the disease confined to the right colon will remain well after resection of the ascending, transverse and descending colon, with anastomosis of the ileum to the sigmoid or rectum. The colitis usually originates in the rectum and progresses in a proximal direction. Since it is difficult to determine where diseased bowel stops and normal bowel begins, transverse colostomy has been unsatisfactory, even for cases in which the colitis seems to be confined to the rectum and sigmoid. Aylett recently reported satisfactory results in 70 per cent of cases following colectomy and anastomosis of the ileum to the rectum. This procedure is based on the belief that the ulcerated rectum will heal, despite its continued use, once the colon has been removed. Other surgeons have had less satisfactory results with this operation. It should be noted that even the 70 per cent of patients with a favorable response rarely have less than four bowel movements a day, and most have five or six. Reactivation of the disease, fistulas and arthritis have occurred. The danger of the development of carcinoma in the rectal segment must also be considered.

Since patients with ulcerative colitis are now operated on before they become moribund, the operative mortality is low, recovery after the operation is rapid, and the total period of hospitalization is not long. They often gain from 25 to 50 lb. within a few months after the ileostomy and colectomy. Today these patients are rarely subjected to more than two operative procedures. In some cases, the rectum as well as the colon may be removed at the time the ileostomy is performed.

In recent years, the complications associated with an ileostomy for ulcerative colitis have been strikingly reduced, and many no longer occur. For example, the immediate application of a temporary ileostomy bag in the operating room at the conclusion of the operative procedure has eliminated the problem of skin irritation around the ileostomy.

The modern ileostomy appliance enables these patients to assume a normal place in society. The bag lies flat against the body and gives no indication of its presence, even under a close-fitting dress. Since it is cemented to the skin, there is no odor. These patients may enter crowded classrooms without embarrassment. In fact, they return to all types of work, take part in athletics, and have a normal life expectancy.

Even though he has an ileostomy, the patient with ulcerative colitis who has been surgically treated is usually most grateful. He will not soon forget the years of chronic weakness, abdominal pain and constant diarrhea. The student may return to school and finish his education. The wage earner is again able to support his family. Although she has an ileostomy, the young woman—now restored to health—is able to marry and have children of her own.

Comment by Dr. Wakefield:

During the course of chronic ulcerative colitis there may arise certain complications which are best treated surgically. These complications are: (1) intractable and uncontrollable rectal hemorrhages, (2) clinically manifest colonic obstruction caused by narrowing or stricturing of the lumen of the colon, (3) adenomatous polyps, and (4) carcinoma, which arises more commonly in adenomatous

polyps or in the colonic wall which has been injured by chronic ulcerative colitis than it does in the normal colon.

Perforations of the colon are not unusual in severely involved colons, but in such situations they usually are subacute and may be more wisely treated conservatively. Cellulitis or an abscess from subacute perforation of the colon during an exacerbation of chronic ulcerative colitis may occur in the abdomen or in the pelvis, and occasionally such an infection involves the perirectal structures, with subsequent formation of multiple fistulas. Often this complication is best treated surgically. The significance of these multiple fistulas contrasts sharply with that of single fistulas occurring in the perianal region. Single perianal fistulas often subside in their degree of activity and may become practically symptomless. They can be treated surgically by the proctologist after healing of the colitis.

In some patients who have ulcerative colitis the symptoms seem to be unremitting. Their health gradually declines until carrying on any kind of work is impossible. Such patients may best be treated surgically. However, intractability in chronic ulcerative colitis is a relative term, because some patients who have intractable ulcerative colitis perform light work regularly and are happy; in others the intractable disease becomes disabling by the time the diagnosis is made. If the patients of the first group would submit to colectomy, they would do well with an ileac stoma; whereas patients of the second group would be more disabled, if such is possible, with an ileac stoma than with the ulcerative colitis.

It is axiomatic that the surgical procedures required for establishment of an ileac stoma and total colectomy are not without some risk. An ileac stoma is not something for a patient to choose just because it is offered to him; it is a handicap to anyone who has it. Proper management of the stoma requires a considerable amount of time. No entirely satisfactory arrangements are known for collecting ileac dejecta. The skin about an ileac stoma requires meticulous care. If the stoma is not properly constructed, the intestine may prolapse through the stoma, the stoma may retreat, or it may become stenosed so that a subsequent operation is needed. Chronic enteritis may be present but remain undiscovered prior to colectomy, and the terminal ileum thus involved may require subsequent resection. The ileum may become involved in adhesions after colectomy, and subsequent operation may be required to relieve intestinal obstruction.

It is my observation from association with experienced surgeons and internists that the longer they are responsible for the care of patients who have chronic ulcerative colitis, the more conservatively they treat those who have this disease. I am sure that most of these patients in the end are grateful for the conservative treatment.

Comment by Dr. Colcock:

There is little to disagree with in Dr. Wakefield's presentation. He has given an excellent résumé of the medical treatment of ulcerative colitis. As already stated, I feel that these patients should be given all that we have to offer in the way of medical treatment. I suspect that, in actual practice, we might disagree as to just when we would consider medical treatment had failed. However, in most instances the patient himself would settle this disagreement. For example, Dr. Wakefield has suggested the use of a diaper (to be changed several times a day) for fecal incontinence. The physical and mental distress associated with this situation would probably have to be experienced to be fully appreciated. It has been my experience that when persistent fecal incontinence develops most patients have been unable to continue in school or to remain at their work. Dr. Wakefield is aware of the limitations of hormone therapy and of the need for surgical intervention when perforation, fistulas or obstruction develops. He also has pointed out the increased danger of carcinoma in patients with long-standing ulcerative colitis. I feel that any patient who has been given a thorough trial on the program which Dr. Wakefield has outlined, and in whom complications develop that cannot be treated by conservative means or who is still unable to work or return to school should be advised to have an operation.

CLINICOPATHOLOGIC CONFERENCE

Report From Veterans Administration Hospital, Hines, Illinois

Edited by William J. Gillesby, M.D., Assistant Chief, Surgical Service

Case Report

A 65 year old white man entered Hines Veterans Administration Hospital on May 1, 1957, complaining of dysuria, frequency and nocturia, nausea, headaches, edema in both legs, and shortness of breath on exertion. These symptoms had been present for three weeks. He had had marked difficulty in passing urine for two days prior to admission, and the urinary stream was very small.

In addition to the usual childhood diseases, the history included a fracture of the right hip, with pinning, 18 months previously; resection of the right testicle, due to injury during childhood; and mild intake of alcohol up to three months prior to admission. One of the patient's sisters died of kidney disease, and his mother died of heart disease. Family history was otherwise not remarkable. The patient had been a gardener and factory worker.

Physical examination revealed that the patient was slightly obese and well developed, with a low voice, slight distention of the neck veins, periorbital edema, bilateral loss of hair from the eyebrows, and dry, bushy hair. There were rales in the bases of both lungs. The heart was enlarged to 2 cm. left of the midclavicular line in the sixth intercostal space. A systolic apex murmur ($A_2 > P_2$) was heard, and blood pressure was 180/100. The liver was just palpable; moderate ascites and 3 plus edema of the ankles were present. Grade 2 prostatic enlargement was found. These findings on admission were thought to indicate hypertensive cardiovascular disease, prostatic hypertrophy with urinary retention, and myxedema.

Hospital course—The presence of glycosuria and elevated fasting blood sugar established a diagnosis of diabetes mellitus, for which the patient received 10 units NPH insulin daily. Persistent albuminuria and the presence of cellular elements, casts and bacteria (several organisms were found on culture), coupled with inadequate visualization of the right kidney and nonvisualization of the left kidney on intravenous pyelography, normal retrograde pyelography, and findings at cystoscopy, led the genitourinary consultant to believe that the patient had pyelonephritis of the left kidney and prostatic hypertrophy.

Bed rest, drainage with the Foley catheter, and administration of diuretics resulted in an 18 lb. weight (edema) loss within a few weeks after admission. Because of persistently low basal metabolic rates, the patient was given small doses of thyroid for myxedema.

Routine x-ray of the chest revealed lesions at the levels of the first and third front ribs on the right side, the suggestion of a small mass in the left hilus, pleural thickening of both bases, and cardiac enlargement. Several masses were identified on the lateral views. To determine a primary source for the metastatic lesions shown on the x-ray of the chest, an upper gastrointestinal series was performed, which

showed a filling defect of the greater curvature of the antrum; gastroscopic examination revealed no abnormalities. Biopsy of the supraclavicular fat pad showed chronic lymphadenitis. Bronchoscopy revealed distortion of the right upper lobe orifice, which prevented visualization of the apical segment orifice. Extrinsic pressure with antral occlusion of the bronchus suggested a tumor in this area. Smear and culture for tuberculosis gave negative results.

On June 27, nitrogen mustard therapy was started (7.5 mg. four times daily). On July 8, x-ray treatments were begun, consisting of 1800 r through each of five ports to the right side of the chest and 1800 r through each of six ports to the left side of the chest. X-ray treatments to the right side of the chest were completed August 21. At this time, some respiratory trouble recurred and the patient had pulmonary edema, for which mercaptomerin sodium was given. On September 3, it was noticed that the patient had decreased reflexes on the right side and some facial weakness, which was interpreted as a transient cerebrovascular episode. On October 9, x-ray of the chest revealed progression of the lesions, and there was a question of pleural effusions. There were rales in the right base and dullness over the left base. X-ray therapy to the left side of the chest was completed on October 10. On November 7, the patient was discharged from the hospital with a diagnosis of metastatic carcinoma (primary site undetermined), diabetes, arteriosclerotic heart disease with myocardial insufficiency, pyelonephritis, and benign prostatic hypertrophy.

On December 11, the patient was readmitted to the hospital because of progressive weakness and shortness of breath. He had marked edema of the lower extremities and genitalia. Blood pressure was 160/110, pulse 78. There was fluid in the left side of the chest and moist rales in the right base. The heart was enlarged to the anterior axillary line ($A_2 > P_2$), and no murmurs were heard at this time. The liver was nontender and was palpable 2 cm. below the costal margin. There was lateral deviation of the left eye and some weakness of the right facial musculature. Tendon reflexes on the right were diminished, and n abdominal reflexes could be elicited. The ci culation time was 58 seconds and the venou pressure 185 mm. of saline.

The patient was placed on a low sodiun diet, and the edema decreased. He became dis oriented and had a transient episode of diar rhea. On January 27, 1958, 500 cc. yellowisl fluid was removed from the left side of th chest. The patient became progressively weak er and died.

Laboratory data—X-ray examination of the chest on May 7 showed a lobulated mass at the level of the first anterior rib on the right side and another mass at the level of the third rib on the right side medially. There also was a suggestion of a small mass in the left hilus and pleural thickening of both bases. The cardiac diameter was increased 15 per cent above the predicted normal. Several masses were identified on the lateral view. The cardiac silhouette from the posteroanterior view suggested double density. This was believed indicative of metastatic malignancy involving the lungs.

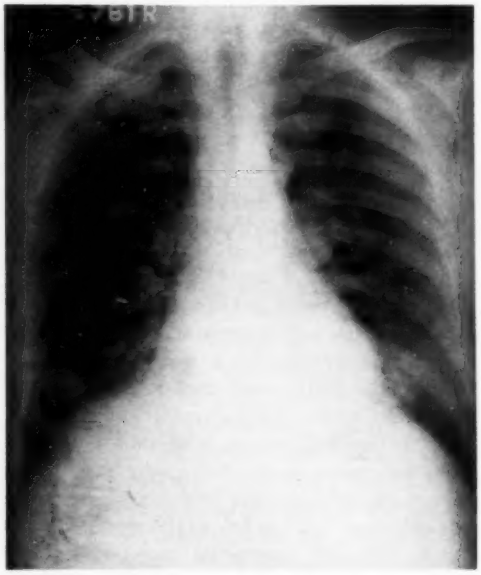

FIGURE 1. X-ray showing a lobulated mass at the level of the first anterior rib on the right side and another mass at the level of the third rib on the right side medially. The heart is enlarged.

with a possibility of bilateral pleural effusion (figure 1).

The same conditions were evident in an anteroposterior Bucky view of the chest made on May 14. In addition, multiple smaller rounded densities were scattered throughout both lung fields, consistent with metastatic malignancy of the lungs. A chest film made on June 7 showed no changes from the previous examination. On September 20, the previously described rounded opacities were again evident by x-ray. A narrow opacity obliterated the right costophrenic angle and extended up to the lateral margin of the right side of the chest. A large homogeneous shadow occupied the left costophrenic angle and extended up to the lateral wall of the left side of the chest (figure 2).

On October 10, x-ray showed progression of the lesions; there had been no significant response to x-ray therapy. A pleural effusion on the left side and increased densities in the right lung field were noted on December 16; on January 14, 1958, an increase was seen in the large homogeneous opacity on the left side. This obscured the left costophrenic angle and extended up to the axillary border. Homogeneous opacities in the right lung field also were more distinct than they had been on previous examinations (figure 3).

An electrocardiogram made on August 9 was interpreted as abnormal, revealing a first-degree auriculoventricular block and nonspecific ST-T wave changes compatible with effects of digitalis or coronary insufficiency or both. Repeated on December 12, the electrocardiogram showed no change from the previous tracing.

On May 15, intravenous pyelography gave inadequate visualization of the right kidney and nonvisualization of the structure of the left kidney. A retrograde pyelogram on May 23 was normal. A gastrointestinal series on May 20 revealed a filling defect of the greater curvature of the antrum, with a normal small bowel. Repeated one week later, the gastrointestinal series was normal. Other laboratory data are summarized in table 1.

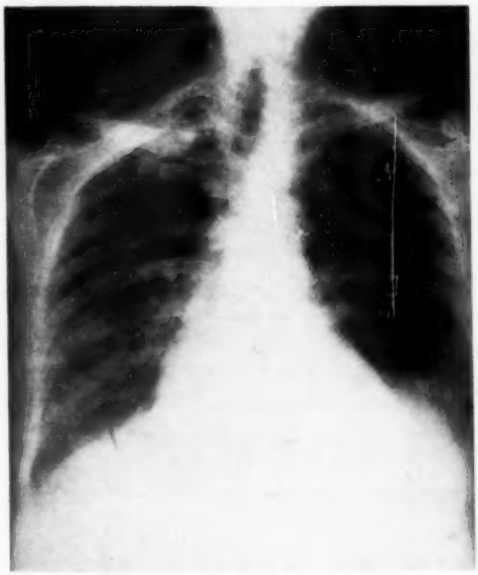

FIGURE 2. X-ray showing conditions similar to those seen in figure 1, with pleural effusion on the left side and clouding of the right lung field.

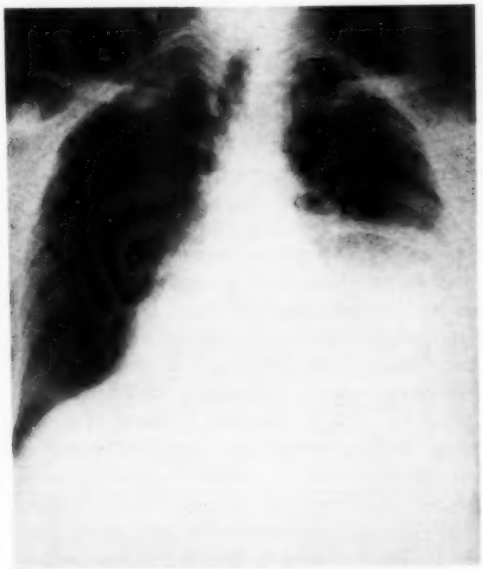

FIGURE 3. X-ray showing a marked increase in pleural effusion on the left side. The masses are more distinct than in figures 1 and 2.

TABLE 1

LABORATORY DATA

TESTS	DATES													
	5/3	5/20	5/29	7/1	7/17	7/22	7/24	7/29	8/28	9/18	10/9	11/6	12/16	1/15
Red blood cell count	4.01		3.71	3.13	2.7									
Hemoglobin	12.		11.	10.	9.	9.5	9.		9.5	9.5	12.5	12		10
Hematocrit	32			30			27			24	29	36		31
White blood cell count	7000		8500	8200	2000	5,950	5200	4200	4,650	5100	4000	5300		3700
Neutrophils	77		69	83			69	89		75	50	79		76
Lymphocytes	23		26	15			31	8		22	48	13		13
Monocytes			2							2		8		10
Eosinophils			2	2				3		1	2			1
Basophils			1											
Platelets				227,000			75,000	155,000						
Sedimentation rate	25													
Sodium	141					136							139	
Potassium	4.05					3.65							4.45	
Carbon dioxide-combining power	21.6					22							19.9	
Chloride	101					102							100	
Nonprotein nitrogen	48.5								38.7		34.7		51.6	
Creatinine									1.8					
Uric acid			7.2											
Glucose	232													
A-G ratio	3.6-2.3												3.1-2.0	
Cholesterol														
Total	196													
Esters	136													
Alkaline phosphatase		15.6	9.7											
Cephalin-flocculation														Neg.
Thymol turbidity														3
Urine														
Specific gravity	1.013		1.010					1.006	1.010					

TABLE 1 *(Continued)*

LABORATORY DATA

TESTS	DATES												
	5/3	5/20	5/29	7/1	7/17	7/22	7/24	7/29	8/28	9/18	10/9	11/6	12/16	1/15
Albumin	4+	4+	3+					2+	3+					
Glucose	4+	0	0						0					
White blood cell count	Few	Few	Many					Many	Few				Many	
Red blood cell count														
Casts		Granular	Hyaline											
Epithelia	Few	Few	Few					Few	Few				Many	
Bacteria	Many	Many						Many	Few				Many	

Basal metabolic rates: –31 per cent, –24 per cent, –19 per cent.

Radioiodine uptake: 15.9 per cent.

Protein-bound iodine[131]: 0.003 mc. per liter (borderline hypothyroid).

Discussion

DR. GORDON L. SNIDER (assistant director, chest department, Michael Reese Hospital, Chicago): This 65 year old man was admitted to the hospital with symptoms consisting primarily of urinary complaints, edema and exertional dyspnea of approximately three weeks' duration. There was an indication of an obstruction to the emptying of the bladder, and the urinary stream was small. On physical examination, the patient was found to be slightly obese and well developed; he had a low voice, slight distention of the neck veins, periorbital edema, bilateral loss of hair from his eyebrows, and dry, bushy hair. These symptoms, particularly the combination of periorbital edema and loss of the hair from the eyebrows (we are not told whether it was a general alopecia of the eyebrows or whether it was confined primarily to the lateral third), would make us think first of myxedema.

The distention of the neck veins and the edema would necessitate determining whether or not this patient was in congestive heart-failure. There were rales in the bases of both lungs, and the patient's heart was enlarged 2 cm. to the left of the midclavicular line in the sixth intercostal space. He had a systolic apex murmur, and the aortic second sound was louder than the pulmonic second sound. Since pulmonary disease was present, I think this latter fact is important. If we were dealing with failure of the right side of the heart secondary to pulmonary hypertension which, in turn, was due to pulmonary disease, the pulmonic second sound would be expected to be at least equal to or perhaps louder than the aortic second sound. I think this immediately indicates that if this was heart disease, it was *associated with* pulmonary disease rather than *due to* pulmonary disease.

The patient had a mild-to-moderate hypertension, with elevation of both systolic and diastolic pressures; the liver was just palpable (we are not told whether or not it was tender). Moderate ascites and 3 plus edema of the ankles were present, and a grade II enlargement of the prostate was found.

The patient was treated for diabetes melli-

tus, which was established by the presence of glycosuria. When the renal disease was investigated, it was found that he had persistent albuminuria, cellular elements, casts and bacteria, with diminished renal function. This was indicated by the fact that at no time on intravenous pyelography was dye excreted by the kidneys; yet, on retrograde examination, there was no evidence of an obstructive uropathy. Four urinalyses recorded during the patient's last illness showed the highest specific gravity to be 1.013. This, with the failure of visualization of the kidneys in the pyelogram, indicated the presence of chronic renal disease.

Are the urinary findings related to the congestive heart-failure, which was noted on admission? In the presence of a very low specific gravity, we cannot reach this conclusion. Ordinarily, the specific gravity would be higher if the renal involvement were due purely to chronic passive congestion. Furthermore, the renal findings would improve somewhat as the heart-failure responded to therapy, which it did temporarily. The patient responded to treatment with mercurials and diuretics and to catheter drainage. He was digitalized, and administration of digitalis was continued throughout the remainder of his illness.

The patient's thyroid status is questioned because his basal metabolic rates were persistently low. We are not told whether or not the various rates were determined before he had lost edema fluid, whether they were calculated on the basis of dry weight, or whether some of the hypometabolism demonstrated by the rates was related to edema. The cholesterol studies were within normal limits. The radioiodine uptake was normal; there was a borderline protein-bound iodine^{131}, indicating that the turnover of iodine was slightly impaired. The patient may well have had some thyroid disease, although myxedema was not perfectly obvious. Was some of the periorbital edema seen in this patient related to chronic renal disease, or was it related to thyroid disease?

At the time, it was believed that the patient had metastatic lesions from a primary malignancy of undisclosed site. A biopsy of the supraclavicular fat pad revealed chronic lymphadenitis. One does not expect to see metastatic disease in these lymph nodes except in a small percentage—perhaps 20 per cent—of all patients with metastatic malignancy of the lung. On the contrary, in chronic granulomatous disease, particularly Boeck's sarcoidosis, the incidence of involvement of the supraclavicular lymph nodes is higher—75 to 80 per cent. Bronchoscopy revealed distortion of the orifice of the right upper lobe. Poor visualization of the apical segmental orifice was interpreted as extrinsic pressure with anterior occlusion of the bronchus, suggesting a tumor in this area. Smear and culture for tuberculosis showed negative results. It is distinctly possible, particularly at the time that this patient was first being studied in May, that he had an occult carcinoma of the bronchus, a very tiny bronchogenic carcinoma which had manifested itself first by metastases rather than by atelectasis or bleeding or by presenting as a mass. We do not know whether or not this man was coughing or wheezing or whether he ever had had any hemoptysis.

Accuracy in diagnosing malignancy will be greatly increased if Papanicolaou smears are done, and I believe that just one examination is insufficient. The experiences of Farber and a number of others, including myself, have indicated that the possibility of finding definitely malignant cells from the Papanicolaou examination is increased by doing a minimum of five examinations. There is a progressive increase in yield from one through five examinations; however, it does not increase appreciably beyond this point. In a series of six or seven examinations, we have had four negative results and one that was unsatisfactory, with the final test in the series showing unequivocal tumor cells. I think this is worthy of comment in terms of the type of investigation which might have been done in diagnosing this case.

The same thing may be said regarding the exclusion of infectious granulomatous diseases, which surely would have to be considered with the findings revealed by the chest roentgenograms in this case. A single culture was done for tuberculosis, and there were no cultural studies for mycotic organisms. I believe we should consider the importance of carrying

out skin tests, particularly the tuberculin test and the histoplasmin skin test, if there is a serious possibility of a tuberculous or a histoplasmic granuloma. Skin tests are less valuable insofar as blastomycosis and coccidioidomycosis are concerned. It might have been of help to have known the geographic areas in which this patient had lived.

Malignancy was diagnosed, and the patient received nitrogen mustard therapy and irradiation. In August, he had an episode of respiratory difficulty and pulmonary edema; treatment with diuretics was apparently successful. A transient episode of involvement of the central nervous system occurred in September, and, in October, the chest roentgenograms were reported to show progression of the lesions. In reviewing these films, I cannot see that the nodular densities on the right have progressed. I think they have changed, but the shadows have undergone some change in contour and there is a question of whether at least one of these lesions has not undergone excavation. One cannot be certain from these films whether or not central excavation had occurred; laminagraphy would be essential to make such a diagnosis. There had been no great increase in the size of the lesions. Since the lesions regressed three times and the effusion disappeared completely between May and October, I think we should consider whether this effusion was due to malignancy, to heart-failure, or to some other process in the lungs. Because of alteration in the lymphatic drainage of the lungs, it is possible that a patient who has metastatic malignant disease of the lungs with associated heart-failure may have effusion localized to the left, as in this case, without involvement of lymphatic structures in the lungs and mediastinum. I have seen such patients respond dramatically to diuretic therapy without ever having had evidence of pleural metastatic complications.

In January, 500 cc. yellowish fluid was removed from the left side of the chest by thoracentesis; however, we are not told whether a cell block or a Papanicolaou smear was made of this material. The yellowish color of the fluid suggests that at one time there was blood in the pleural fluid. This, together with the history and the roentgenologic findings in the patient, who was in heart-failure, would indicate to me a serious possibility of pulmonary infarction. One would wonder whether the process that had occurred at the left base may not have been of the nature of recurrent pulmonary infarcts.

The patient had marked edema of the lower extremities and genitalia when he was readmitted to the hospital in December. Again, there was a disproportion between what we would consider to be the underlying mechanism of the edema and the physical findings. At this time, the blood pressure was 160/110, essentially the same as at the first admission. The pulse, however, was 78. There is an indication that the patient had sinus rhythm with a first-degree auriculoventricular block. He was digitalized. A pulse rate at this level can be seen in a digitalized patient with heart-failure, but, again, I think we should ask ourselves if this was edema on a renal basis. The cardiac findings were essentially unchanged, except that no murmurs were now heard. The liver was enlarged, and this time it was noted that it was nontender. We now have an indication of central nervous system involvement and definite evidence of congestive heart-failure in the elevated venous pressure and prolonged circulation time. Apparently, the patient died in intractable heart-failure.

In summary, this patient had pulmonary disease which was manifested as pleural involvement of the right apex, pleural disease at both bases, and pleural effusion at the left base, with a number of nodules on the right side and one or two very tiny ones in the left lung. That these did not progress throughout eight or nine months does not seem compatible with the course of malignant disease; in the absence of other definite histologic evidence from either a bronchoscopic examination or Papanicolaou smears, I am very reluctant to make such a diagnosis.

It is conceivable that the patient may have had chronic pyelonephritis associated with hypertension and heart disease, but at no time did he have uremia. There may have been associated arteriosclerotic heart disease. I have indicated that insofar as the lungs are con-

cerned, there are various granulomatous diseases which can present this sort of picture: tuberculosis, histoplasmosis, tularemia, blastomycosis, and a long list of others which we can rule out only by cultural studies. Indeed, in diagnosing this case, it would be best to have the pathologist make special stains with the tissue and, perhaps, have the bacteriologist work simultaneously on additional material. I cannot explain the renal lesion as being caused by either tuberculosis or any of the other chronic infectious granulomas I have mentioned. There is no evidence of cavitary lesions in the kidney, which we generally but not necessarily would expect to see. I would find it difficult to tie together the cardiac, renal and pulmonary lesions into a single disease entity.

There is one entity which does incorporate the pulmonary disease, the renal lesion, the involvement of the heart, and the possible involvement of the thyroid gland. It is Wegener's granulomatosis, which is characterized by granulomatous lesions of the respiratory tract, a generalized focal necrotizing vasculitis involving vessels of the lungs and of other organs, and finally by a glomerulitis with necrosis and thrombosis of the capillary tufts of the glomerulus and evolution in the kidney of the granulomatous lesions.

Many features of this case do not fit entirely into this disease entity. There was relatively little evolution of the pulmonary lesions; and there was no upper respiratory tract involvement; however, the latter may or may not be present in Wegener's granulomatosis. Furthermore, this patient's hospital course was largely afebrile, and most patients with Wegener's granulomatosis are febrile. Despite these factors, I believe that Wegener's granulomatosis is the most likely diagnosis if one is to incorporate the entire disease picture into a single etiologic entity. This is the reason I questioned the development of cavitation in the right midlung field. In such instances, the pleural effusion may well be secondary to pulmonary artery thrombosis with pulmonary infarction and subsequent resolution of the infarcts. The heart can be involved in this condition, which would help to explain the cardiac enlargement and intractable heart-failure in the absence of obvious evidence of arteriosclerotic heart disease superimposed on hypertension. Finally, I think the renal findings of persistent albuminuria, the persistence of red and white blood cells, and the occasional showers of casts would best be explained by this picture. As mentioned previously, this condition also includes possible involvement of the thyroid and other organs, which this patient may have had.

DR. I. E. KIRSH (staff physician, radiology service): I am interested in the methods by which circumscribed peripheral masses in the lung can be diagnosed. This matter commonly confronts radiologists, internists and surgeons. The surgeons and the pathologists generally have the last word, for in many cases an accurate diagnosis cannot be made without resection. There are two widely publicized and contradictory views on this subject. Some investigators maintain that x-ray gives no particular information, while others contend that x-ray reveals a great deal of information. My opinion is somewhere between these two theories. I would say that x-ray sometimes shows important findings.

There are certain procedures that can be followed. As suggested by Dr. Snider, body section x-rays (laminagraphy) may be helpful. Practically speaking, if a substantial amount of stippled calcification is seen within the mass, it very likely indicates a granuloma, not a neoplasm. Granuloma is most often tuberculoma, but it can be histoplasmoma. Body section x-rays also may be helpful in finding cavitation or rarefaction within the mass; however, a neoplasm and a granuloma can cavitate centrally and thus not be seen by laminagraphy. X-ray also shows changes in the size and shape of a mass; however, by the time growth is observed, it is too late. The mass should be excised before it starts to grow.

The lack of progress of the lesions in this patient is not what one would expect of a neoplasm; however, certain metastatic masses, such as those originating in the thyroid, do not show great growth over a period of time. There is one other complication in this case. Instead of having a single circumscribed mass, this patient had two circumscribed masses.

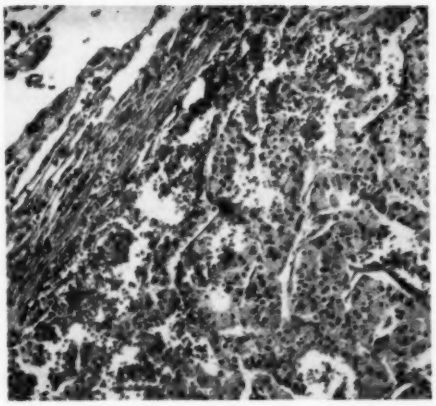

FIGURE 4. Photomicrograph of the carcinoid type of bronchial adenoma, with proliferation near the vascular channels.

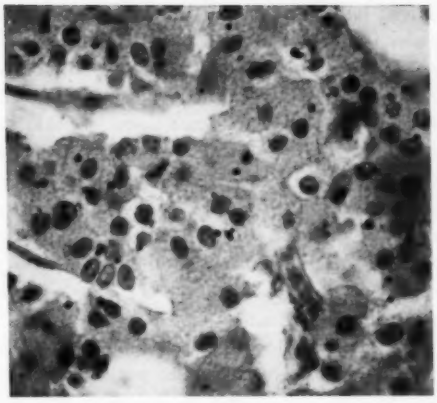

FIGURE 5. Higher-power photomicrograph of the carcinoid bronchial adenoma.

This seemed to indicate immediately to us that the condition was metastatic carcinoma, and I guess we stopped thinking at this point. Of course, it is possible to have both a malignant circumscribed mass and a benign circumscribed mass, or both may be benign. We thought that the condition in this patient was in the class of multiple circumscribed masses and, therefore, that it was malignant.

DR. SNIDER: I meant to mention primary amyloidosis, which could conceivably cause these symptoms. However, renal involvement is not common in this condition, although it does occur in secondary amyloidosis. I had not considered it in relation to primary (not secondary) amyloidosis.

DR. MYRON E. RUBNITZ (chief of pathology): Hydrothorax, with 1000 cc. fluid, was found in the left pleural cavity. Absence of the fluid in the right pleural cavity is explained by the fact that the cavity was obliterated. The patient's heart weighed 500 gm., which is almost two times the normal size. Patchy areas of fibrosis in the myocardium attested to the fact that the patient probably had old small myocardial infarcts. The important pathologic finding was an old 2 cm. caseous nodule in the right apical area; 2 or 3 cm. below this was another nodule which also was about 2 cm. in diameter, but, instead of being caseous, it was bulging and pinkish-red.

Particularly interesting was a yellowish-white nodule, approximately 3 cm. in diameter, which was found in the liver. The kidneys were slightly contracted and granular, a condition that we would recognize grossly as arteriosclerotic. The thyroid weighed 15 gm. and showed nothing abnormal. The autopsy was allowed only for the chest and abdomen, so we do not know if there was any metastatic involvement.

The lower lesion in the right upper lobe proved to be a bronchial adenoma, and the lesion above that was described grossly as an old tuberculous lesion. Special stains failed to divulge any evidence of acid-fast bacilli, but there was no suggestion of any other type of granulomatous lesion.

Bronchial adenomas are somewhat unusual; according to some statistics, they constitute about 6 to 10 per cent of primary lung tumors. From the great numbers of bronchogenic cases seen at this hospital, it is evident that this type of tumor is found equally in both sexes, while bronchogenic carcinoma is said to occur five times more frequently in men. Statistics indicate that 85 per cent of bronchial adenomas occur in persons less than 50 years of age. (This patient was 65, so he does not qualify for this group.) Such tumors ordinarily are divided into two histologic types: the so-called carcinoid type and the cylindroid type. This

patient had a carcinoid tumor. The carcinoid tumor is not considered as malignant-appearing as the cylindroid, nor does it extend into or invade the surrounding parenchyma. This lesion is distinguished from bronchogenic carcinoma in that there usually are no alterations or necrosis, and the fibrous or desmoplastic reaction seen in bronchogenic carcinoma does not occur in carcinoid tumor. Microscopically, the cells in the carcinoid tumor are seen in sheets and in strands, and very often around small vascular channels (figures 4 and 5).

The caseous nodule in this patient, which was uppermost, had calcific material with a definite capsule around it. Grossly, this also was very well encapsulated and suggestive of tuberculoma.

The bronchial adenoma showed proliferation about some of the vascular channels. In more proximally occurring bronchial adenomas in which biopsy has been attempted, this vascularity has caused some patients to bleed profusely.

This patient also had bronchopneumonia. It was of the nodular type in that it was not completely confluent and involved mainly the lower lobes.

The appearance of the kidney lesion was very characteristic of diabetic glomerulosclerosis, which we know better as the Kimmelstiel-Wilson syndrome and which is believed to be a specific for a diagnosis of diabetes mellitus. In other words, it does not occur in any other condition. It has been reported to occur in about one-third of those diabetic patients who are more than 40 years of age, but it very rarely is found in patients less than 30. If there are only a few of these lesions in the kidneys, there usually are very few symptoms or findings. With widespread evidence of diabetic glomerulosclerosis, any or all of these symptoms may be present. This patient was hypertensive. It is not stated whether or not he had retinopathy. He did have albuminuria and edema, and although he did not have hypercholesteremia, he had many of the symptoms. A study of the glomeruli and the surrounding kidney parenchyma in this particular disease shows that the so-called afferent arteriole is the involved vessel; because it increases the tension in the glomerulus, it is said to cause hypertension.

The hyalinization often found in the pancreas of diabetic patients is in no way related to the hyaline lesions in the glomerulus; thus there may or may not be changes in the pancreatic islets. Other than some fibrosis and fatty infiltration, this patient had very few changes in the pancreas.

The capillary lesions found in the kidneys are not seen in other areas in the body. This is particularly true in the great number of peripheral vascular diseases which result from diabetes; the changes generally are in the larger vessels.

Diabetic glomerulosclerosis represents a sclerosis of the walls of the glomerular capillaries, not of the supporting stroma. The liver nodule which was found in this patient was a typical hemangioma about 3 cm. in diameter. This particular lesion is seen much more commonly in women than in men. The average age at which it occurs in men is 62 years. Among the many theories concerning the origin of hemangioma is the contention that it may in some way be due to an increase in female sex hormones. Angiomatous lesions often develop in various areas of the body in pregnant women. Most of these lesions are solitary, small and symptomless, and they fibrose with increasing age. These were the characteristics of the lesions in this patient. He actually had a number of different lesions. Coincidentally, two of them were in the same lobe of one lung, which possibly accounted for the many types of treatment he received.

DR. SNIDER: I would like to make several further comments. I think that the most important consideration in relation to the diagnosis which I made is that factor which bothered me most; namely, that this patient had an afebrile course throughout his illness, and Wegener's disease is usually a febrile disease.

Prior to this discussion, I asked if an effort had been made to examine chest films taken of this patient before his last illness. I believe it is the policy of most veterans' installations to make survey films on admission, although a man admitted with a fractured hip could easily have escaped such a survey. In-

vestigation probably would have shown, however, that x-rays were made of this patient at the time of his separation from the service, and, if it could have been demonstrated that the masses were present at that time and had remained unchanged, the diagnostic error might not have occurred. I also would like to ask the pathologist if this adenoma could have been reached endoscopically for biopsy, which would have established the diagnosis.

DR. RUBNITZ: The growth could not have been reached endoscopically, because it was peripherally placed, as is more common with the carcinoid type of tumor than with the cylindroid type.

DR. W. J. GILLESBY (assistant chief, surgical service): I would like to ask what caused this patient's death and if a serotonin test might have helped establish the diagnosis of carcinoid tumor.

DR. RUBNITZ: I think the patient probably died of pneumonia. In relation to the serotonin test, I want to point out that the name "carcinoid pulmonary type of adenoma" pertains only to the description of the cell and not to the argentaffin granules which the ordinary carcinoid of the gastrointestinal tract usually contains. Only a minute percentage of stains for argentaffin granules are ever positive. Thus, these tumors are called carcinoid only because of the appearance of these cells, not because of any relationship to the lesions of the gastrointestinal tract.

DR. SNIDER: This is generally true; however, there was a recent report of a case of carcinoid adenoma with the symptom complex of serotonin excretion. This was in a patient who had asthma and valvular heart disease. Thus, it can occur, although it is exceedingly rare. The patient we are discussing had none of these symptoms.

DR. RUBNITZ: Ordinarily, adenomas are solitary and benign tumors. However, they apparently may be multifocal in origin, and rare cases of malignant adenomas have been reported in the literature.

Postgraduate Clinical NOTES

111. CONSULTATION

The art of consultation was not simply a question of sending a patient away for a second opinion. It was the careful selection of the man who by training and temperament was the most suitable for the matter in hand. His position in the profession, his standing in his specialty, his skill, his appearance, his manner, and his gift of tongues had all to be considered. When a consultant and a general practitioner met, no matter how distinguished the one or how obscure or diffident the other, they met on terms of absolute equality, the one to give, the other to receive, but not necessarily to adopt, the advice tendered. The consultant had to be careful here. He should be patient while the practitioner told his tale; he should not wave away, as of no account, the x-rays that had been brought; and he should not, with a brisk, "Well, I don't think we need discuss this together, need we?" deprive the practitioner of the opportunity to consider what was to be said to the patient, before it was said. Beyond all doubt a consultation was of immense value to the general practitioner, for it afforded him priceless opportunities of keeping up to date.

G. F. Abercrombie, The art of consultation, *British Medical Journal*, November 29, 1958, p. 1349

CLINICAL STUDY

Acetyldigitoxin: Digitalization With a Single Orally Administered Dose

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ACETYLDIGITOXIN, a chemically pure crystalline glycoside, was derived by Stoll and Kreis[1] through enzymatic removal of a single glucose molecule from naturally occurring lanatoside A (obtained from *Digitalis lanata*). The cardiotonic action of acetyldigitoxin is rapid in onset, and the glycoside is absorbed well from the gastrointestinal tract.[2,3] Early reports suggested that with this preparation gastrointestinal symptoms of digitalis overdosage appear before signs of cardiac toxicity,[3-13] and that these symptoms disappear more quickly on cessation of acetyldigitoxin therapy than they do following treatment with digitoxin.[14]

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This report summarizes our experience at the Los Angeles County Hospital, where we used a single orally administered dose of acetyldigitoxin to digitalize 21 patients with heart disease of various causes.

Method

In the 21 patients studied, acetyldigitoxin was used when a patient had congestive heart-failure or atrial fibrillation with rapid ventricular response, or both. Most of these patients had not previously received any type of

digitalis preparation; the few who had been given digitalis had not received any for at least 30 days prior to the start of this study. In addition to digitalization, the usual methods of controlling congestive failure were followed, such as bed rest and sodium restriction. Mercurial diuretics, morphine, aminophylline and ammonium chloride were given as indicated. Paracentesis was unnecessary in these patients.

In most instances, base-line electrocardiograms were obtained before therapy was initiated. All patients were rapidly digitalized with a single dose of orally administered acetyldigitoxin. As earlier experiences[15] with this drug in a small series of cases suggested that the single orally administered digitalizing dose is between 1.8 and 2.2 mg., these limits were observed in this study, except in the case of patient No. 4, who received 2.0 mg. initially and a second dose of 1.0 mg. approximately 18 hours later. Dosage was adjusted on the basis of weight and body size: Patients of average weight received an initial dose of 2.0 mg.; smaller patients received 1.8 mg., and larger patients received 2.2 mg. The daily maintenance dosage of acetyldigitoxin was 0.2 mg. in all but patient No. 20, whose maintenance dosage was increased to 0.3 mg. on the third day of therapy (table 1). Effects of treatment were charted throughout the period of hospitalization, but no attempt was made to observe the patients for longer periods.

Effects of therapy were checked at least once in each 24 hour period by at least two observers. Changes in weight were noted, and in some instances arm-to-tongue circulation times were determined with DECHOLIN®. Apical pulse rates were noted in the resting recumbent patient. If arrhythmias were suspected, electrocardiograms were taken. An attempt was made to chart the rapidity of therapeutic response. Any suggestion of toxicity was carefully investigated.

Description of Patients

Age, sex, diagnosis and therapeutic response are summarized in table 1. Included in the study were 11 patients with arteriosclerotic heart disease, eight patients with hypertensive heart disease, one patient with rheumatic heart disease, and one patient with syphilitic heart disease. Atrial fibrillation was present in nine of the 21 patients.

Results

Acetyldigitoxin's rapid action was most apparent in the patients with atrial fibrillation. In one patient who had atrial fibrillation, marked slowing of the pulse rate—from 130 to 80 per minute—occurred within six hours; in two patients the ventricular rate was lowered significantly in 12 hours, and in another patient good response—a decrease from 110 to 60 per minute—resulted within 24 hours.

Two patients required a larger than usual dose of acetyldigitoxin. An 80 year old woman who had arteriosclerotic heart disease, atrial fibrillation and congestive heart-failure had an apical pulse rate of 120 per minute on admission. An initial dose of 2.0 mg. acetyldigitoxin was administered orally, but a check seven hours later disclosed an apical rate of 134 per minute. Eighteen hours after the initial dose, the pulse rate was recorded at 140 per minute, and an additional 1.0 mg. acetyldigitoxin was given. Three hours after the second dose, the pulse rate had fallen to 88 per minute. On the following day, an electrocardiogram demonstrated multiple premature ventricular contractions, and acetyldigitoxin was discontinued. Four days later, after all evidence of toxicity had disappeared, the patient was placed on a maintenance dosage of 0.2 mg. per day. Throughout this entire period the clinical course had improved steadily, with no gastrointestinal symptoms of toxicity. This patient died suddenly on the tenth hospital day.

The second patient who required more than the usual dose of acetyldigitoxin was a 54 year old man with hypertension, atrial fibrillation and severe congestive heart-failure. At the start of therapy, his ventricular rate was 150 per minute. He was given 2.2 mg. of acetyldigitoxin. The following day, his pulse rate was 140 per minute, and he was placed on a maintenance dosage of 0.2 mg. per day. On the third day of hospitalization, he experienced profuse diuresis and felt markedly

TABLE 1

CLINICAL DATA ON PATIENTS TREATED ORALLY WITH ACETYLDIGITOXIN

PATIENT	AGE AND SEX	CARDIAC STATUS	DOSAGE		RESULTS
			Initial (mg.)	*Maintenance (mg.)*	
1	67 M	Hypertension with massive CHF	2.0	0.2	Pulse rate reduced from 108 to 85 per minute in three days; weight reduced 30 lb. in three weeks; pulse reduced to 75 per minute in six days; excellent response.
2	72 M	Calcific aortic stenosis with hydrothorax and anasarca	2.0	0.2	Pulse rate reduced from 108 to 88 per minute in 24 hours; appetite good; weight reduced more than 16 lb. in six days; good response.
3	75 F	Hypertension with possible MI and mild CHF	2.0	0.2	Pulse rate reduced from 88 to 68 per minute in five days; appetite good; patient did well; discharged on fifth day.
4	80 F	ASHD with atrial fibrillation and CHF	2.0 1.0	0.2 (after four days)	Initial pulse rate of 120 per minute before digitalization increased to 134 per minute seven hours later; additional dose of 1.0 mg., administered 18 hours after first dose, reduced pulse rate to 88 per minute in three hours; on following day, patient had multiple PVCs (confirmed by electrocardiogram); appetite good; PVCs cleared in four days; patient placed on 0.2 mg. maintenance dosage, but died suddenly on tenth day.
5	63 F	Hypertension with CHF	1.8	0.2	Pulse rate reduced from 130 to 110 per minute on day following digitalization; excellent diuresis; improvement rapid; pulse rate remained between 90 and 95 per minute.
6	59 F	Rheumatic aortic stenosis and CHF	2.0	0.2	Pulse rate reduced from 92 to 64 per minute in two days; good diuresis; appetite fair.
7	69 M	Calcific aortic stenosis; atrial fibrillation and hydrothorax	1.8	0.2	Pulse rate reduced from 110 to 60 per minute in one day; excellent subjective improvement; no toxicity.
8	77 M	ASHD; atrial fibrillation and mild CHF	2.2	0.2	Pulse rate reduced from 100 to 80 per minute in one day; profuse diuresis; good result in mild failure.
9	73 M	Calcific aortic stenosis; atrial fibrillation and mild CHF	1.8	0.2	Pulse rate reduced from 120 to 63 per minute in 12 hours; appetite good; patient did well; discharged two days later.
10	75 F	ASHD; atrial fibrillation; anasarca	2.2	0.2	Prior to treatment, electrocardiogram showed atrial fibrillation at 120 per minute; after treatment, pulse rate was 60 per minute with occasional PVCs; patient never ate well, and died suddenly on tenth day.
11	68 M	Diabetes; hypertension; severe MI; gallop rhythm	1.8	0.2	Pulse rate reduced from 120 to 85 per minute on day following digitalization; gallop disappeared; appetite good; patient died suddenly on tenth day.
12	51 M	Severe hypertension and left ventricular failure	2.0	0.2	Following digitalization, pulse rate reduced from 90 to 70 per minute in one day; PVCs, noted before and after digitalization, cleared on maintenance dosage in six days; excellent subjective response; questionable transient toxicity.
13	55 F	Uremia and CHF	2.0	0.2	No appreciable change in pulse rate in three days; good diuretic response; appetite good.

TABLE 1 *(Continued)*

CLINICAL DATA ON PATIENTS TREATED ORALLY WITH ACETYLDIGITOXIN

PATIENT	AGE AND SEX	CARDIAC STATUS	DOSAGE		RESULTS
			Initial (mg.)	*Maintenance (mg.)*	
14	67 M	Old MI and mild left ventricular failure	2.2	0.2	Following digitalization, pulse rate reduced from 100 to 68 per minute in four days; appetite remained poor, but no other evidence of toxicity; clinical response fair.
15	56 M	Hypertension; atrial fibrillation; anasarca	2.2	—	Pulse rate reduced from 132 to 85 per minute 12 hours after digitalis; in 24 hours rhythm had converted to sinus with 10 PVCs per minute; no further digitalis administered; PVCs cleared in two days; weight reduced 19 lb. in two weeks; good response, with transient toxicity.
16	83 M	ASHD; left ventricular failure; multiple PVCs	1.8	0.2	Base-line electrocardiogram showed multiple PVCs; pulse rate reduced from 100 to 75 per minute three days after digitalization, with few PVCs; pulse rate 80 per minute with no PVCs after five days of maintenance dosage; appetite fair; clinical response good.
17	69 F	ASHD; atrial fibrillation and mild CHF	2.0	0.2	Pulse rate reduced from 140 to 90 per minute in 16 hours, falling to 85 per minute on following day; appetite good; good clinical result.
18	85 F	ASHD; atrial fibrillation and mild CHF	1.8	0.2	Pulse reduced from 130 to 80 per minute six hours after start of therapy; appetite good; excellent, rapid response.
19	83 M	Hypertension; acute MI; anasarca	2.0	0.2	Pulse rate reduced from 100 to 80 per minute; good diuresis, but failure cleared slowly; appetite only fair; patient died on ninth day with severe chest pain.
20	54 M	History of hypertension; atrial fibrillation; severe CHF	2.2	0.2 0.3	Pulse rate reduced from 150 to 140 per minute in one day; good diuresis and subjective improvement on second day of therapy; pulse rate 100 per minute; dosage increased to 0.3 mg. per day on third day and maintained until patient's discharge seven days later; patient much improved and edema-free, but pulse rate never fell below 100 per minute.
21	67 M	Luetic heart disease with aortic insufficiency and anasarca	2.2	0.2	Initial pulse rate 112 per minute; excellent diuretic response, but pulse remained at 90 per minute; good result.

CHF—Congestive heart-failure
ASHD—Arteriosclerotic heart disease
MI—Myocardial infarction
PVC—Premature ventricular contraction

improved. As his ventricular rate remained at 100 per minute, the maintenance dosage of acetyldigitoxin was increased to 0.3 mg. per day and was continued at this level until he was discharged seven days later. Although this patient was much improved and edema-free, his pulse rate did not fall below 100 per minute.

Good response in the presence of chronic left ventricular failure with multiple ectopic ventricular contractions is illustrated by patient No. 16. The base-line electrocardiogram of this 83 year old man showed a ventricular rate of 100 per minute with numerous ectopic ventricular beats. A single orally administered dose of 1.8 mg. acetyldigitoxin reduced the

rate to 75 per minute. The patient was placed on a maintenance dosage of 0.2 mg. Three days later good clinical response was noted, and ectopic ventricular contractions were less frequent. When the patient was discharged after seven days' hospitalization, his pulse rate was 80 per minute and no ectopic ventricular contractions were recorded.

Toxicity

Questionable evidence of toxicity was present in four of the 21 patients. In patient No. 4, discussed previously, the total dosage was 3.0 mg. in two days. Toxicity was manifested by multiple ectopic ventricular contractions, which persisted for four days despite temporary discontinuance of acetyldigitoxin. The patient's appetite remained good and from the fifth to the tenth day no other signs of toxicity were noted, although a maintenance dosage of 0.2 mg. digitalis was resumed. At that time the patient died suddenly.

Possible toxic reactions occurred in three additional patients, all of whom received the maximal digitalizing dose (2.2 mg.) used in this study. In patient No. 10, who had rapid atrial fibrillation, the rate was reduced from 120 to 60 per minute in three days, but occasional ectopic ventricular beats were noted on the electrocardiogram. This patient never ate well, but no nausea or vomiting occurred.

Patient No. 15 had atrial fibrillation with rapid ventricular response; his apical rate prior to treatment was 132 per minute. The day after digitalization with 2.2 mg. acetyldigitoxin, the fibrillation had been converted to sinus rhythm, but 10 ectopic ventricular contractions per minute were noted. Digitalis was discontinued for two days, and the ectopic ventricular contractions disappeared. Over-all clinical response was good, and no gastrointestinal toxicity was evinced.

Patient No. 19, an 83 year old man with myocardial infarction and congestive failure, had only fair ventricular response, but diuresis was good and the congestive failure cleared slowly. His appetite was fair. This patient died suddenly during an episode of chest pain on the ninth day of treatment.

In each of the four cases, evidences of toxicity were questionable and insufficient to warrant discontinuing acetyldigitoxin therapy

Comment

Our experience in this study indicates the feasibility of producing digitalization with a single orally administered dose of 1.8 to 2.0 mg. acetyldigitoxin. This glycoside appears to be absorbed rapidly from the gastrointestinal tract and is capable of producing dependable cardiotonic effects. Satisfactory clinical response was obtained in all patients studied. Evidences of toxicity appeared in four of the 21 patients. In each instance the patient had received more than 2.0 mg. of the drug. Toxicity was manifested mainly by ectopic ventricular beats which subsided rapidly—in two to four days—after acetyldigitoxin was discontinued. Anorexia was noted, but no nausea, vomiting or other form of gastrointestinal toxicity was encountered. These findings do not agree with the work of Doherty,[16] in that the dosages in these patients were higher and the incidence of toxicity was smaller.

Summary and Conclusions

1. Digitalization with minimal side effects can be obtained by oral administration of a single 1.8 to 2.0 mg. dose of acetyldigitoxin.
2. With dosage levels higher than 2.0 mg., toxic side effects are much more frequent.
3. Toxicity manifested by disturbance of rhythm was more common than gastrointestinal toxicity, but all toxic effects subsided in two to four days after the drug was stopped.
4. Individualizing the dosage is important. When properly used the drug appears to be a dependable and effective therapeutic agent.

ACKNOWLEDGMENT

We wish to thank Mr. Harry Althouse, Sandoz Pharmaceuticals, San Francisco Division of Sandoz, Incorporated, Hanover, New Jersey, for supplies of acetyldigitoxin (ACYLANID®) used in this study and for the material aid which made the study possible.

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MEETINGS *and Postgraduate Courses*

American Academy of Pediatrics, San Francisco: Spring session, April 13-15, Sheraton-Palace Hotel. For further information, write to: Executive Office, American Academy of Pediatrics, 1801 Hinman Avenue, Evanston, Ill.

American Orthopsychiatric Association, San Francisco: Thirty-sixth annual meeting, March 30-April 1, at the Sheraton-Palace Hotel. For further information, write to: Dr. I. N. Berlin, Cochairman, Public Relations Committee, Langley Porter Neuropsychiatric Institute, San Francisco 22.

Biological Photographic Association, Iowa City: Midwestern sectional meeting, April 24-26, at the University of Iowa. For further information, write to: Margaret S. Ames, 640 East Armour, Kansas City 9, Mo.

International Academy of Proctology, New York: Eleventh annual convention, April 5-9, at the Plaza. For further information, write to: International Academy of Proctology, 147-41 Sanford Avenue, Flushing, N.Y.

International College of Surgeons, Chicago: The division of obstetrics and gynecology announces its second annual competition for two awards of $500 and $300 each for the best manuscripts on a phase of obstetrics and gynecology. Contest is limited to: interns, residents or graduate students in obstetrics and gynecology, and those engaged in practicing or teaching the specialty. Manuscripts must be submitted on or before June 1, 1959. For further information, write to: Dr. Harvey A. Gollin, 55 East Washington Street, Chicago 2.

Medical Library Association, Toronto, Ontario: Medical library refresher course on June 13 and annual convention on June 15 at the King Edward Sheraton Hotel. For further information, write to: Miss Ruth Mann, Mayo Clinic Library, Rochester, Minn.

The World Medical Association, Montreal, Quebec: Thirteenth general assembly, September 7-12. For further information, write to: Secretary General, World Medical Association, 10 Columbus Circle, New York 19.

Tufts University School of Medicine, Boston: Postgraduate courses for 1959:
Hematology, April 9-11
Electrocardiography, April 13-17
Neurology, April 29-May 2
For further information, write to: Dr. Robert P. McCombs, Postgraduate Division, Tufts University School of Medicine, 171 Harrison Avenue, Boston 11.

University of Washington School of Medicine, Seattle: Postgraduate courses for 1959:
Seminars on common neurologic problems, April 13-14
Fractures of the extremities, April 27-28
Corticosteroid therapy, May 20-22
Blood coagulation workshop, June
Common emotional problems in children and adolescents, June 25-27
Practical psychiatry, July 20-24
Pediatric allergy and recent advances in care of newborn infants, September 17-19
Fluid and electrolyte balance, September 23-26
Neurologic problems in childhood, October
Obstetrics and gynecology, October
Arrhythmias, November
For further information, write to: Division of Postgraduate Medical Education, University of Washington School of Medicine, Seattle 5.

Editorials

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THE FIRST SYMPTOM

WHEN a doctor inquires of his patient as to the first symptom noted in relationship to the disturbances which have brought him to the doctor, the answer is exceedingly important from a diagnostic point of view. Dr. C. G. Learoyd[1] believes that any invasion of the human body by microorganisms, any disturbance of hormonal balance, or any cell proliferation should in some manner be recognized by the mind. However, many conditions which attack human beings are insidious in their onset, and, obviously, the mental threshold varies with different persons. Pain is often a late symptom. Dr. Learoyd is convinced that subtle changes have occurred in the mind long before clamant pain. For instance, a man who has an incipient corn will begin taking a bus, where previously he walked, long before the existence of the corn reaches his consciousness as pain. "For hundreds of years," says Dr. Learoyd, "it has been noticed that a sense of well-being precedes an attack of gout, but the well-being is of a particular kind, a full-barn feeling with the testiness of power and much meanness in it, which in reality is due to the mobilizing of urates et al. in the blood." He has found that similar but distinctive expansiveness precedes an attack of fibrositis. He believes also that metabolites in muscle cause a particular kind of mental stimulus which results in exercise, the primal object of the mental stimulus being to remove those metabolites by exercise. Also profoundly philosophical is his comment, "In nine cases out of 10 the first symptom which is essentially protective will ward off the disease, but when it fails to do so, even by the learned it will be indicted as the cause."

The stream of consciousness, according to Dr. Learoyd, "is the most delicate gauge of health and any disease or poisoning will show itself first by causing a regression in the mode of thought." This is the only way the mind can act in adversity.

I found especially interesting the introspective observations made by Dr. Learoyd about the common cold. He says, "Like most, I do occasionally suffer from that viral invasion which is called 'a common cold.' Hours before the first sneeze, which itself is hours before the feel of battle for the nasopharynx, I get certain mental changes: Familiar places, an office or a sitting room, become dreary and loathsome and have a smell about them, which

is a child's and savage's way of labeling localities; familiar faces assume the Hogarthian touch; strange, of the earth earthy and rather repellent, memories of the open air, Rugger and the sailing of small boats, whiffs of woodland, moor and fen present themselves, and the habit of fantasy, almost purposefully forgotten in most adults, comes back and weaves around these subjects. Nature is saying, wisely or unwisely, 'Go for a five mile walk, man!' Later come the fantasies which depict a paradise of warmth and solitude where one would be, but, if one can obey them, before long the vivid-coloured adventure fantasies come back and urge. Much later, when the bacteria and cocci have joined in the fight, their poisonous and thought-restricting action makes the picture confused. Robert Graves wrote of his 'flu' in 'Good-bye to All That': 'My temperature was running high now and my mind was working clearly as it always does in fever. My visual imagery, which is cloudy and partial at ordinary times, became defined and complete.'

"Even that amount of volunteered insight is rare, but dozens of people have been asked about this and those who are intelligent enough to understand and introspect have given a great variety of answers with broad similarities, and in most the utilitarian hand of function is apparent. My point is that before a cold could even be a suspicion of a cold there are changes in that most delicate gauge, the stream of consciousness."

The observations of Dr. Learoyd are in the best tradition of the great clinicians. Fascinating are some of the observations relative to changes of a cyclothymic into a manic phase. One woman would put on a black silk dress just before a manic attack; another woman would always ask for a third cup of tea, and a third always asked the doctor for a cigarette. These are physical signs of tensions which had been building up for weeks. The experienced superintendent in a private mental hospital saw a group of patients walking on parole. One of them walked across an oval of grass instead of going around it. This departure from routine indicated the start of an attack.

Dr. Learoyd concluded that the first symptom of any disease must be a mental one. He feels that rheumatoid arthritis, cancer and similar conditions are long preceded by changes in the delicate stream of thought. All the processes involved are obviously not yet known and certainly not established. The concept itself is still in the realm of speculation, but from such fundamental speculations eventually come new pathways into knowledge of the greatest possible significance.

MORRIS FISHBEIN

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THE FUTURE OF RESEARCH

A special committee appointed by the secretary of the U. S. Department of Health, Education, and Welfare has reported that expenditures for medical research in the United States can and should be tripled to reach $1 billion a year by 1970. With this recommendation came a warning that there must be a major increase in the number of physicians and other scientists engaged in medical research, rising from approximately 20,000 now engaged to 45,000 by 1970.

The chairman of the committee was Dr. Stanhope Bayne-Jones, formerly dean of the Yale University School of Medicine and now president of the Joint Administrative Board of the New York Hospital-Cornell Medical Center. The committee felt that it would not be in the public interest for the number of physicians in the nation to fall below the ratio of 132 for each 100,000 persons. This is the ratio which has prevailed over the past 30 years. The construction of from 14 to 20 new medical schools at a cost of between $500 million and $1 billion would be necessary to maintain this ratio. The committee pointed out that about 10 years are required from the time a school is planned until the first class graduates.

In 1957 the federal government expended $186 million for medical research. The comparison between amounts spent for research in 1953 and 1957 by various federal agencies is shown in figure 1. Figure 2 shows the com-

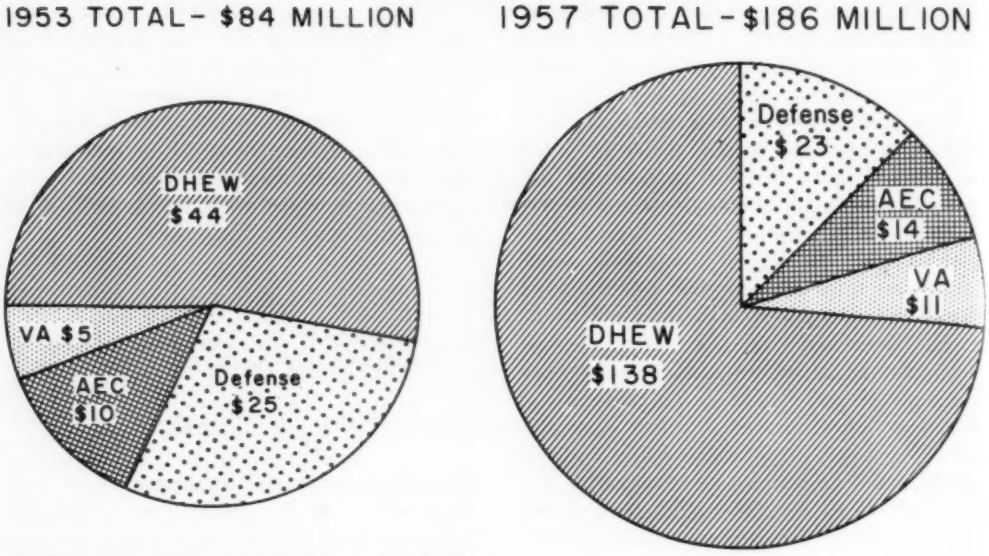


FIGURE 1. Support of medical research by federal agencies.

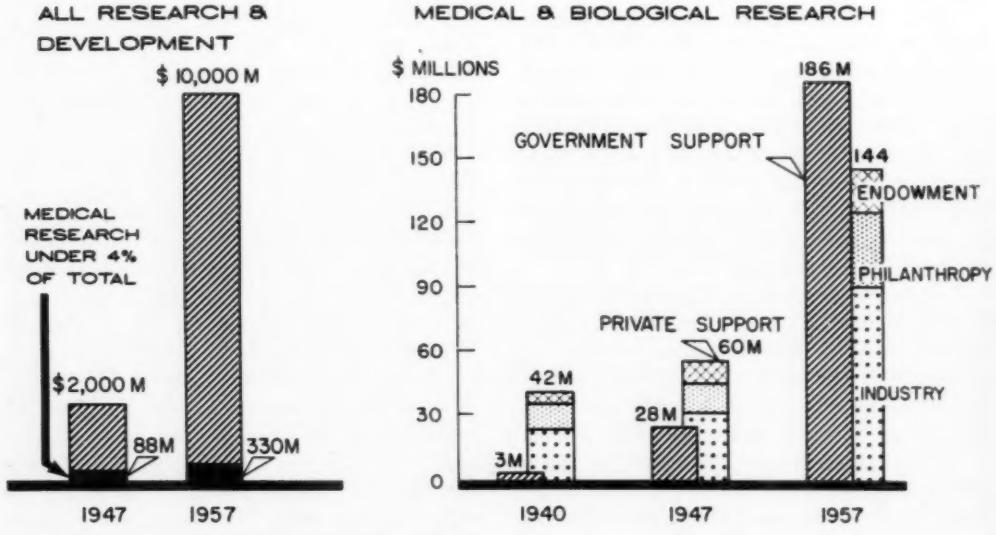
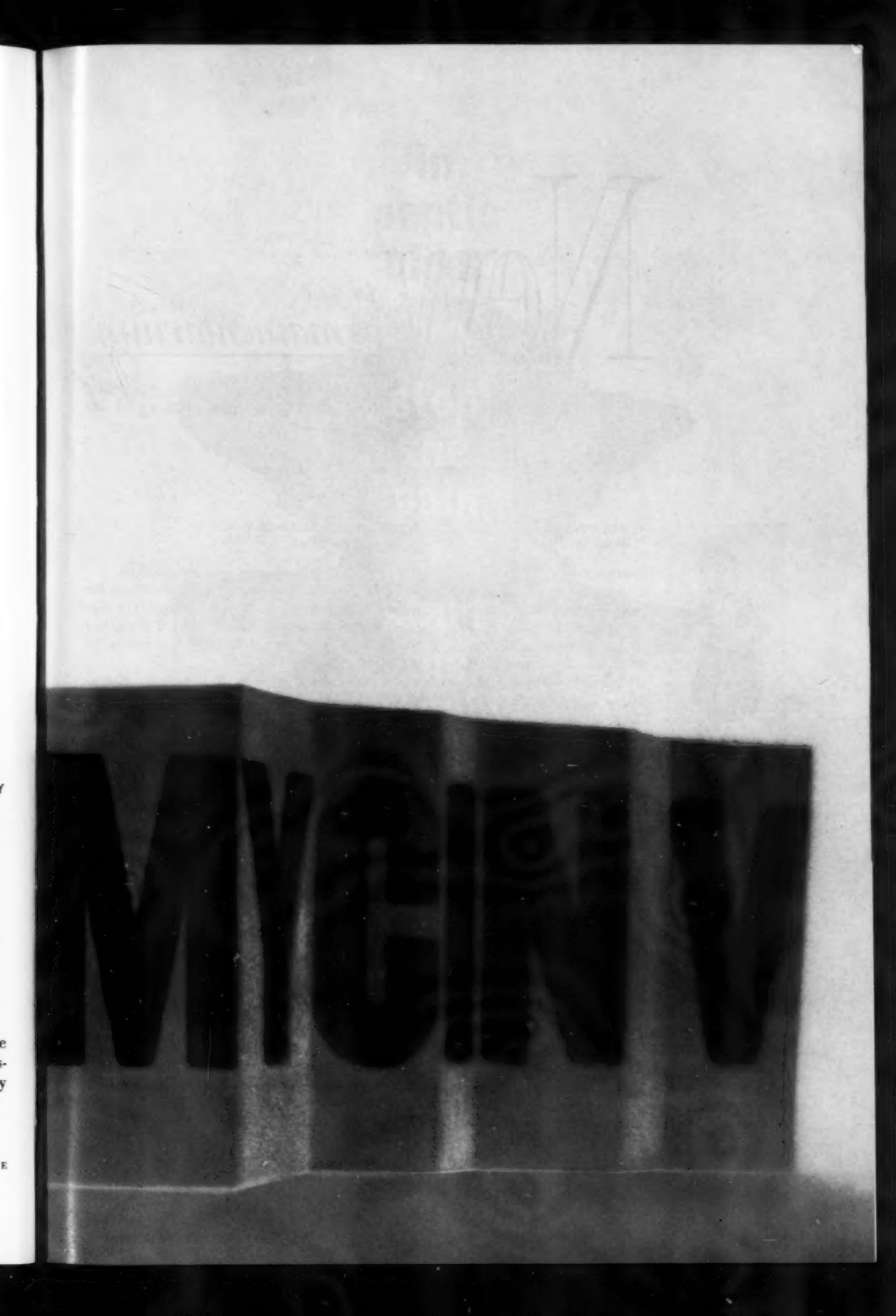


FIGURE 2. Research funds before and after World War II.

parison in the 1940, 1947 and 1957 expenditures for medical research by private philanthropy, industry and endowments; the amount spent by all sources on total research was $10 billion. The committee recommended that by 1970 the government increase its expenditure for medical research to $500 million, industry to $300 million, and private philanthropy to $100 million.

MORRIS FISHBEIN


MYCIN

New *for your armamentarium*

Information published in this department is supplied by the manufacturers of the products described.

• WELL COUNTER (Model SC-1)

DESCRIPTION: Incorporating a transistor-equipped preamplifier, this well-type scintillation counter detects all levels of gamma radiation in prepared samples. As little as 10^{-5} μc I^{131} may be detected with a counting efficiency of about 50 per cent. A 2⅛ in. lead shield reduces background counts to about 200 per minute under average conditions. Other features include a counterbalanced lid with handles, removable plug over crystal for long test tubes and samples up to 22 cc., and two piece construction for easier handling. The instrument measures 17 by 10 in., and weighs 220 lb.
PRODUCER: Nuclear Measurements Corporation, Indianapolis.

• DUMOGRAN®

PURPOSE: Tissue-building hormone therapy.
COMPOSITION: Tablets contain methyltestosterone, ethinyl estradiol, vitamins and minerals.
INDICATIONS FOR USE: Menopause, male climacteric, tissue wasting and chronic debility.
HOW SUPPLIED: Bottles of 60 and 250.
PRODUCER: E. R. Squibb & Sons, division of Olin Mathieson Chemical Corporation, New York.

• POLY-VI-SOL® AND DECA-VI-SOL® (New Dosage Form)

PURPOSE: Vitamin supplements for children.

These liquid orange-flavored preparations for older children (up to nine years of age) are supplied in 4, 8 and 12 oz. bottles. Poly-Vi-Sol contains six vitamins; Deca-Vi-Sol contains 10 vitamins.
PRODUCER: Mead Johnson & Company, Evansville, Ind.

• HIBITANE® LOZENGES

PURPOSE: To treat mouth or throat infections.
COMPOSITION: Each lozenge contains 5 mg. chlorhexidine dihydrochloride and 2.5 mg. benzocaine.
DOSAGE AND ADMINISTRATION: 3 or 4 lozenges per day as needed.
HOW SUPPLIED: Packages of 12.
PRODUCER: Ayerst Laboratories, New York.

• DERONIL®

PURPOSE: Corticosteroid therapy.
COMPOSITION: Dexamethasone (9-alpha-fluoro, 16-alpha-methyl-prednisolone).
HOW SUPPLIED: 0.75 mg. tablets in bottles of 50 and 500.
PRODUCER: Schering Corporation, Bloomfield, N. J.

(Continued on page A-12?)

KOLANTYL® with 4 needed healing actions

1. **vital antispasmodic action**—BENTYL®—Merrell's fast, safe antispasmodic . . . relieves spasm-pain promptly, without atropine-like side effects. 2. **balanced acid-neutralizing action**—magnesium oxide and aluminum hydroxide—prompt, long-lasting relief . . . no laxation, no constipation. 3. **demulcent action**—Methylcellulose—soothing protective coating covers ulcerated area, promotes healing. 4. **antienzyme-antipepsin action**—Sodium Lauryl Sulfate—effectively curbs necrotic effects of pepsin and lysozyme . . . prevents further erosion. **Dosage**—Gel: 2 to 4 teaspoonfuls every 3 hours, or as needed. Tablets: 2 tablets (chewed for more rapid action) every 3 hours, or as needed. **NON-CONSTIPATING . . . NON-LAXATING**

TRADEMARKS: "BENTYL," KOLANTYL®

Merrell

THE WM. S. MERRELL COMPANY
New York • CINCINNATI • St. Thomas, Ontario
Another Exclusive Product of Original Merrell Research

• MULTIPLE PATTERN VISUAL FIELD SCREENER

DESCRIPTION: Three minute screening tests for glaucoma are now possible with this device. With one eye covered, the patient faces a white screen in a semidarkened room and fixes his uncovered eye on a black dot in the center of the screen. A quarter-second flash of ultraviolet light makes visible a pattern of dots and crosses. If the patient fails to see these images, a complete examination should be made to determine whether or not glaucoma is present.
PRODUCER: Burton Manufacturing Company, Santa Monica.

• MODUTROL

PURPOSE: To provide tranquilizing, anticholinergic and antacid action.
COMPOSITION: Each tablet contains:

l-Piperidine-ethanol benzilate hydrochloride (Sycotrol)	2 mg.
Scopolamine methylnitrate	1 mg.
Magnesium hydroxide	200 mg.
Aluminum hydroxide	200 mg.

INDICATIONS FOR USE: Peptic ulcer and other functional gastrointestinal disorders.
DOSAGE AND ADMINISTRATION: Four times daily.
HOW SUPPLIED: Bottles of 50.
PRODUCER: Reed & Carnrick, Jersey City, N. J.

• REGULATOR HOLDERS

DESCRIPTION: This die-cast aluminum wall holder for oxygen therapy regulators is equipped with three stainless steel screws for mounting and is available with commercial, Canadian or medical thread. It measures 3¼ in. in diameter.
PRODUCER: Ohio Chemical & Surgical Equipment Co. (A division of Air Reduction Company, Inc.), Madison, Wis.

• PEDIATRIC CHEST RUB

COMPOSITION: Camphor, menthol and eucalyptol.
DESCRIPTION: Available in stick form, the medication can also be used as an inhalant by cutting off 1 in. of the stick and placing it in either a vaporizer or a bowl of boiling water.
PRODUCER: Johnson & Johnson, New Brunswick, N. J.

• SIMRON®

PURPOSE: Treatment of iron-deficiency anemia.
COMPOSITION: Each capsule contains 10 mg. ferrous gluconate and an absorption agent.
DOSAGE AND ADMINISTRATION: 1 capsule three times per day between meals.
HOW SUPPLIED: Bottles of 100.
PRODUCER: The Wm. S. Merrell Co., Cincinnati.

• FOOD SERVICE CONVEYER (Model CFS 20C)

DESCRIPTION: Of stainless steel construction, unit has separate compartments for hot and cold food. Refrigeration is provided by cold air generated by a ¼ H.P. compressor and distributed by a circulating blower. Heating is effected by a 500 W tubular sheathed element. Each of seven removable aluminum drawers provides service for three patients. Both hot and cold compartments have removable, nontilt aluminum trays. Three 5 qt. insulated beverage containers have thermostat-controlled heating units. Conveyor features a magnetic door latch and has 8 in. sealed bearing casters and protective encircling bumpers. It measures 29½ by 72½ by 50 in. Model CFS 20B has refrigerant cartridges suspended between the cold compartments.
PRODUCER: The Colson Corporation, Chicago.

(Continued on page A-126)

The picture of health—no "angina problem"

(2 years post-infarct)

...on Metamine Sustained, b.i.d.[1]

When anginal episodes persist in spite of E.C.G. evidence of "good recovery" from myocardial infarction, METAMINE SUSTAINED provides ideal protective medication. In fact, METAMINE SUSTAINED protects many patients refractory to other cardiac nitrates,[2] reducing the number and severity of anginal attacks, or eliminating them entirely. Dosage is easy to remember: "1 tablet on arising, and 1 before the evening meal."

Each tablet of METAMINE SUSTAINED slowly releases 10 mg. of aminotrate phosphate (LEEMING), the long-acting coronary vasodilator virtually free of nitrate side effects (nausea, headache, hypotension).[2] And, when you prescribe METAMINE SUSTAINED your angina patient will need less nitroglycerin and thus remain fully responsive to that vital emergency medication.

Supplied: bottles of 50 and 500 sustained-release tablets. Also: METAMINE (2mg.); METAMINE (2mg.) WITH BUTABARBITAL (1/4 gr.); METAMINE (10 mg.) WITH BUTABARBITAL (3/4 gr.) SUSTAINED; METAMINE (10 mg.) SUSTAINED WITH RESERPINE (0.1 mg.).

Thos. Leeming & Co. Inc. New York 17.

1 tablet all day

1 tablet all night

1. Einfelder, H.W.: Case history 4/35. Personal communication. 2. Fuller, H.L. and Kassel, L.E.: Antibiotic Med. & Clin. Therapy, 3:322, 1956.

• FASCO X-RAY FILM HANGER

DESCRIPTION: Precision hinges snap this stainless steel film hanger firmly in place. The film positions itself at the required angle when placed in the film channel of the frame. The hanger is available in all standard sizes from 5 by 7 in. to 14 by 17 in.; special sizes may be ordered.
PRODUCER: Stirrup Metal Products Corp., Newark, N. J.

• THIOPENTAL SODIUM POWDER

PURPOSE: Anesthetic.
DOSAGE AND ADMINISTRATION: Intravenously.
HOW SUPPLIED: 50 and 250 cc. vials.
PRODUCER: Philadelphia Ampoule Laboratories, Philadelphia.

• SEBULEX®

PURPOSE: Therapeutic shampoo.
COMPOSITION: Sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate, dioctyl sodium sulfosuccinate, KEROHYDRIC® (dewaxed fraction of lanolin), 2 per cent sulfur, 2 per cent salicylic acid and 1 per cent hexachlorophene.
INDICATIONS FOR USE: Itchy, scaly scalp with tendency toward dryness.
DOSAGE AND ADMINISTRATION: Lather shampoo into hair, massage for five minutes and rinse out; repeat procedure.
HOW SUPPLIED: 4 fl. oz. bottles.
PRODUCER: Westwood Pharmaceuticals, division of Foster-Milburn Company, Buffalo.

• COTHERA® COMPOUND

PURPOSE: Symptomatic relief of colds and sinus congestion.
COMPOSITION: Each 5 cc. contains:

Dimethoxanate hydrochloride (Cothera)	25 mg.
Isothipendyl hydrochloride (THERUHISTIN®)	2 mg.
l-Phenylephrine hydrochloride	5 mg.
Acetaminophen	100 mg.
Ammonium chloride	100 mg.
Sodium citrate	50 mg.
Chloroform	0.25%

The compound contains 10 per cent alcohol.
DOSAGE AND ADMINISTRATION: For adults, 1 to 2 teaspoonfuls three or four times a day; for children two to eight years old, ½ to 1 teaspoonful three or four times a day.
HOW SUPPLIED: 16 fl. oz. and 1 gal. bottles.
PRODUCER: Ayerst Laboratories, New York.

• PICKER 2950 CLINICAL SCALER

DESCRIPTION: Designed to measure radiation in nuclear medicine, this unit incorporates a built-in timer that may be preset, three direct-reading plug-in scales, mechanical register, precision discriminator and linear amplifier. The resolving time is less than five microseconds. High-voltage regulation gives stability in discrimination level.
PRODUCER: Picker X-Ray Corporation, White Plains, N.Y.

• HORMOZYME

PURPOSE: Vitamin and hormone supplement for geriatric patients.
COMPOSITION: Each tablet contains: 0.67 mg. HALOTESTIN®, 0.15 mg. ethinyl estradiol, vitamins A and D, thiamine mononitrate, riboflavin, pyridoxine hydrochloride, cyanocobalamine, ascorbic acid, nicotinamide, calcium pantothenate, folic acid and 100 mg. calcium phosphate, dibasic.
CAUTION: Contraindicated for patients with malignancies which may be hormone-dependent.
DOSAGE AND ADMINISTRATION: Usual dosage is 3 tablets daily.
HOW SUPPLIED: Bottles of 100.
PRODUCER: The Upjohn Company, Kalamazoo, Mich.

(Continued on page A-128)

In Asthma

The Most Important Word to Remember...

Medihaler

automatically measured-dose aerosol medications

Nonbreakable • Shatterproof • Spillproof • Leakproof

Available with either epinephrine or isoproterenol

Medihaler-EPI

Epinephrine bitartrate, 7.0 mg. per cc., suspended in inert, nontoxic aerosol vehicle. Contains no alcohol. Each measured dose contains 0.15 mg. epinephrine.

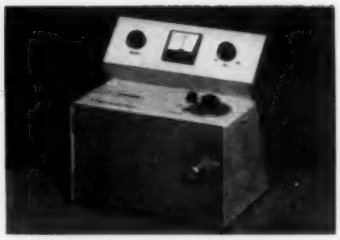
Medihaler-ISO

Isoproterenol sulfate, 2.0 mg. per cc., suspended in inert, nontoxic aerosol vehicle. Contains no alcohol. Each measured dose contains 0.06 mg. isoproterenol.

NOTABLY SAFE AND EFFECTIVE FOR CHILDREN, TOO

Riker

NORTHRIDGE, CALIFORNIA



• FLUOROMETER

DESCRIPTION: This instrument is used to identify and measure concentrations of heavy metal poisons or ADRENALIN® in urine, to measure contamination in water, and for other medical and toxicologic tests. Sensitivity ranges as low as 5 by 10^{-4} quinine sulfate. Use of the unit requires only balancing the null meter with a knob calibrated in 1 per cent divisions. Quantitatively repeatable readings may be made, and calibration is required only when desired because of variability in chemical processing. Either 2537 or 3600 A. lamps may be used. The device operates on 117 V, 50 or 60 cycle AC and requires no transformers, galvanometers, batteries or external light sources.
PRODUCER: G. K. Turner Associates, Palo Alto, Calif.

• VELROC PLASTER BANDAGES

DESCRIPTION: The smooth texture and extra-fast setting time of these bandages make them ideal for casts where ease of application and removal, polished appearance and speed are important.
HOW SUPPLIED: 2, 3, 4, and 6 in. widths, all 3 yd. long.
PRODUCER: Hospital Division, Johnson & Johnson, New Brunswick, N. J.

• DOXICAL

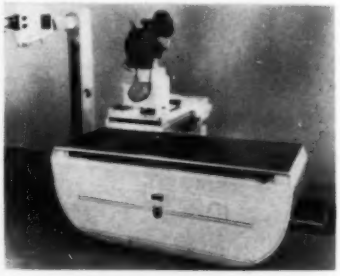
PURPOSE: Fecal softener.
COMPOSITION: Each capsule contains calcium bis(dioctyl sulfosuccinate).
DOSAGE AND ADMINISTRATION: For adults, one 240 mg. capsule; for children more than six years of age, one to three 50 mg. capsules.
HOW SUPPLIED: 240 mg. capsules in bottles of 15 and 100; 50 mg. capsules in bottles of 30 and 100.
PRODUCER: Lloyd Brothers, Inc., Cincinnati.

• DIUPRES®

PURPOSE: Wide-range antihypertensive action.
COMPOSITION: Each tablet of Diupres-500 contains 500 mg. chlorothiazide (DIURIL®) and 12 mg. reserpine; each tablet of Diupres-250 contains 250 mg. Diuril and 125 mg. reserpine.
DOSAGE AND ADMINISTRATION: Adjusted according to patient's needs.
PRODUCER: Merck Sharp & Dohme, division of Merck & Co., Inc., Philadelphia.

• NASAL CANNULA

DESCRIPTION: The disposable polyvinyl chloride tip featured with this cannula eliminates need for daily cleaning or sterilization. A simple snap connection fastens the nontoxic tip to the cannula tube from the oxygen cylinder regulator or wall-outlet flowmeter. Ready-to-use tips may be obtained in packages of 12.
PRODUCER: The National Cylinder Gas Division of Chemetron Corporation, Chicago.



• NORELCO IMAGE INTENSIFIER

DESCRIPTION: This 9 in. unit, with a 63 sq. in. field, permits fluoroscopic observation over large areas and provides images 1500 times brighter than those formerly possible. Thus, daylight fluoroscopy is more practical and less hazardous. The optical system permits viewing by one or two observers and simultaneous recording of images on 35 or 16 mm. movie film. The high intensity facilitates closed-circuit television transmission. Full-size radiographs or movie-radiographs can be made under fluoroscopic control; the spot-film device is free for instant operation.
PRODUCER: Medical and Dental Division, North American Philips Company, Inc., New York.

(Continued on page A-132)

ENARAX one tablet at breakfast
one tablet at bedtime

full-time relief in

peptic ulcer	gastritis	duodenitis
functional bowel syndrome	gastroenteritis	hiatus hernia (symptomatic)
ulcerative colitis	pylorospasm	genitourinary spasm
biliary tract dysfunctions	cardiospasm	dysmenorrhea

Each ENARAX tablet contains:
Oxyphencyclimine HCl . . . 10 mg.,
Hydroxyzine HCl (ATARAX®) . . . 25 mg.

Dosage: One-half to one tablet twice daily – preferably in the morning and before retiring. The maintenance dose should be adjusted according to therapeutic response. Use with caution in patients with prostatic hypertrophy or glaucoma.

Supplied: In bottles of 60 black-and-white scored tablets.

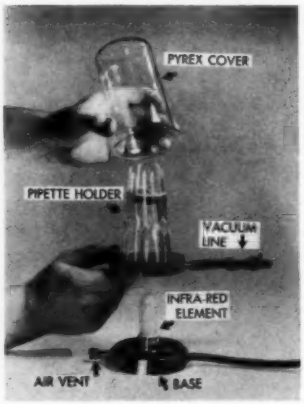
References: **1.** McHardy, G., et al.: Paper presented at Postgraduate Course in Gastroenterology, University of California School of Medicine, San Francisco, California, January 27, 1958. **2.** Strub, I. H., and Carballo, A.: To be published. **3.** Schuller, E.: Gaz. des Hôpitaux *10*:391 (Apr. 10) 1957. **4.** Farah, L.: Internat. Rec. Med. *169*:379 (June) 1956. **5.** La Barre, J.: Compt. rend. Soc. Biol. (Paris) *150*:1807 (Oct.) 1956. **6.** Harrisson, J. W. E., et al.: Paper presented at the 4th Pan-American Congress of Pharmacy and Biochemistry, Washington, D. C., November 3-9, 1957. **7.** Data in Roerig Medical Department files.

ROERIG Rx

New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being

• DYNOPTIC TRIOCULAR MICROSCOPE

DESCRIPTION: In addition to inclined binocular eyepieces, this instrument has a monocular tube for camera attachment which allows simultaneous photomicrography or observation by a second person. The design allows 80 per cent of the source illumination to be directed to the monocular camera tube, while high-intensity microscope illuminators assure sufficient remaining light for visual operation. The triocular body doubles normal magnification and can be rotated 360 degrees for accurate orientation of the specimen in relation to the picture frame.
PRODUCER: Bausch & Lomb Optical Co., Rochester, N.Y.



• MICROPIPET WASHER-DRIER (Model WD-1)

DESCRIPTION: This vacuum-operated unit washes and dries 12 pipets simultaneously. Reduced air pressure draws the washing and rinsing solutions through the pipets, permitting high-speed drying at room temperature without recondensation. The unit consists of a 4⅛ in. drier base with a quartz infrared element operating on 110 V, AC-DC line; a pipet holder; and a PYREX® glass cover. A threaded air vent containing a filter also is provided. Either distilled water or ether-alcohol solutions may be used for the final rinse.
PRODUCER: Micro-Metric Instrument Company, Cleveland, Ohio.

• FARR ASPIRATOR

DESCRIPTION: Featuring a unique foot-pedal action, this portable unit requires no electricity. Although pumping may be interrupted, the high vacuum remains constant, and an especially designed valve controls overflow and prevents pump flooding. This 10 lb. unit provides sufficient suction to clean out thick material deposits, can be set up in less than one minute, and functions equally well indoors or outdoors.
PRODUCER: Conitech, Ltd., Chauncey, N.Y.

• STENISONE

PURPOSE: Corticosteroid therapy.
COMPOSITION: Product contains:

Prednisone	5 mg.
Methandriol	20 mg.
Antacid agents	366.6 mg.

HOW SUPPLIED: Bottles of 30 and 100 tablets.
PRODUCER: Organon Inc., Orange, N. J.

• DOXIDAN

PURPOSE: Laxative.
COMPOSITION: Each capsule contains 50 mg. 1,8-dihydroxy-anthraquinone and 60 mg. calcium bis(dioctyl sulfosuccinate).
DOSAGE AND ADMINISTRATION: For adults, one or two capsules; for children aged 6 to 12, one capsule.
HOW SUPPLIED: Bottles of 30 and 100.
PRODUCER: Lloyd Brothers, Inc., Cincinnati.

(Continued on page A-134)

Squibb announces a new, topically superior anti-inflammatory steroid

Kenalog-S

SPECTROCIN

Squibb Triamcinolone Acetonide with Neomycin and Gramicidin (Spectrocin)

Lotion

with added antibacterial protection

Kenalog-S is a new, clinically superior topical corticoid lotion with added protection against bacterial infection to rapidly relieve itching, inflamed or infected skin lesions.

1. Provides effective anti-inflammatory, antipruritic, antiallergic action for rapid symptomatic relief.
2. Produces clinical results superior to hydrocortisone.
3. Extremely well tolerated—no edema, no electrolyte imbalance or systemic toxicity.
4. 92% effective . . . typical of clinical reports, Kenalog-S Lotion proved 92% effective in 67 patients with various dermatologic disorders.*
5. Attacks pyogenic infections . . . protects against secondary infections . . . with the proved antibacterial action of Spectrocin (neomycin and gramicidin).
6. The consistently effective results and the excellent spreading ability permits supplying of Kenalog-S Lotion in 7.5 cc. economy packages.

and a companion to Kenalog-S

Kenalog Triamcinolone Acetonide **for topical application in dermatotherapy**

Effectively provides prompt symptomatic relief as well as control of most common dermatologic disorders.

Kenalog Cream, 0.1%—5 Gm. and 15 Gm. tubes
Kenalog Lotion, 0.1%—15 cc. plastic squeeze bottles
Kenalog Ointment, 0.1%—5 Gm. and 15 Gm. tubes

*Monographs on Therapy 3:137 (Nov.) 1958

SQUIBB *Squibb Quality—the Priceless Ingredient.*

"KENALOG" IS A SQUIBB TRADEMARK

• AMBU RESUSCITATION-SUCTION KIT

DESCRIPTION: Consisting of a hand-operated resuscitator and a foot-operated suction pump with carrying case, this portable unit requires no electricity or compressed gas. The resuscitator includes an anesthesia-type breathing bag, a nonrebreathing valve, face mask, and three Berman airways, each a different size. The bag is available with an additional valve for administering supplemental oxygen. The pump has an accordion bellows and a plastic trap bottle with a spare overflow valve in the stopper. Each element of the kit may be purchased separately.
PRODUCER: Air-Shields, Inc., Hatboro, Pa.

• PEDIATRIC NASAL DECONGESTANT

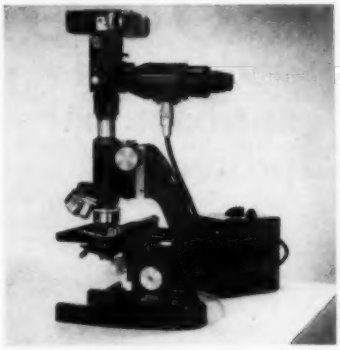
COMPOSITION: Phenylephrine hydrochloride.
DESCRIPTION: This preparation is available in a two-way plastic squeeze bottle, which can be used for either drop or spray administration. A plastic calibrated dropper helps assure accurate drop dosage.
PRODUCER: Johnson & Johnson, New Brunswick, N. J.

• FURACIN® CREAM

PURPOSE: Topical and vaginal antibacterial.
COMPOSITION: Preparation contains 0.2 per cent nitrofurazone (Furacin) in a cream base.
CAUTION: Medication should be discontinued if sensitization occurs.
DOSAGE AND ADMINISTRATION: For vaginal use, 1 full applicator twice daily until healing is complete; for topical use, apply directly or on gauze, repeating application every few days.
HOW SUPPLIED: 3 oz. tubes with plunger-type vaginal applicator.
PRODUCER: Eaton Laboratories, Norwich, N.Y.

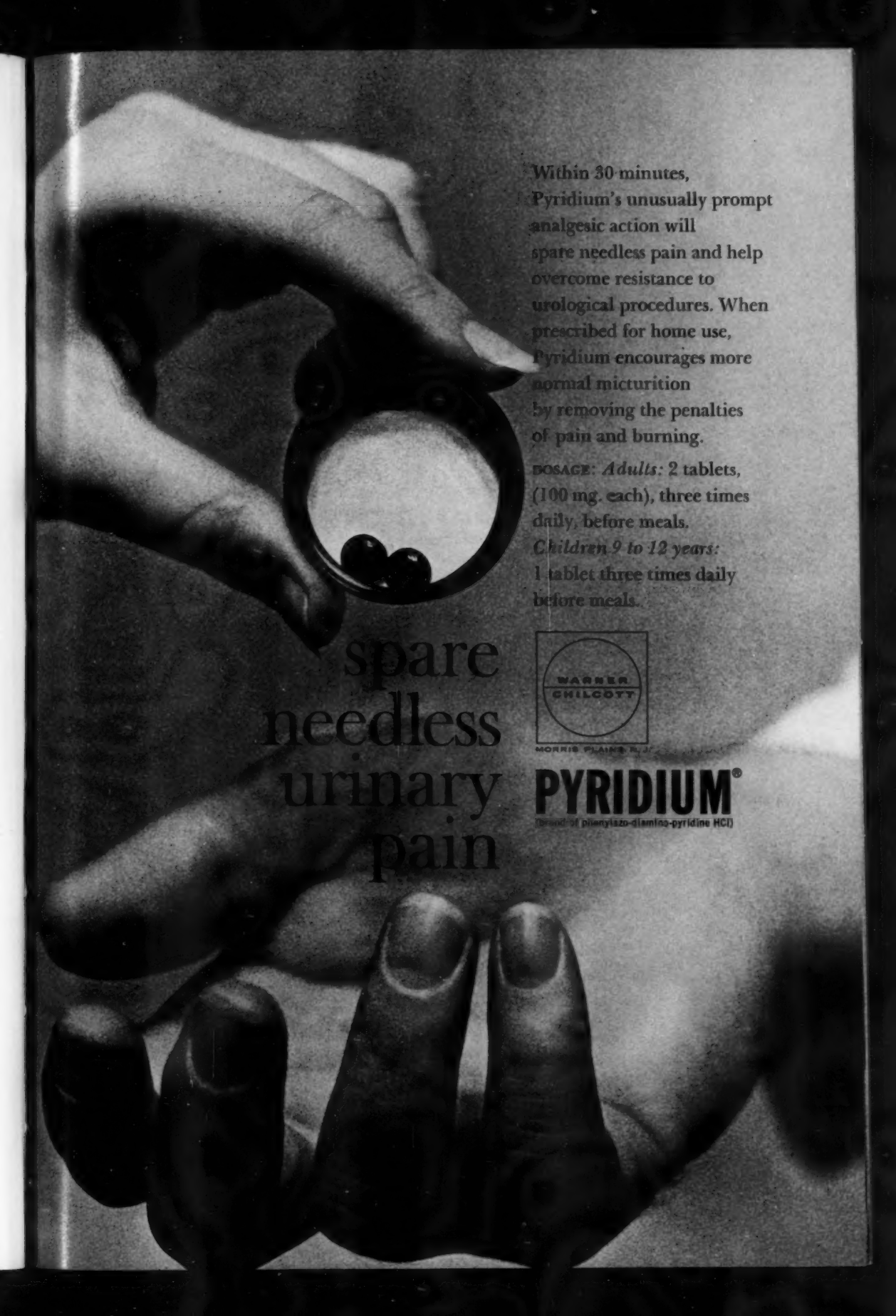
• STEREOCAMERA ATTACHMENT

DESCRIPTION: Designed for use with the Cyclop tic stereoscopic microscopes, the unit consists o a 35 mm. GRAFLEX® stereocamera and an adapte with a special prism compensating system. Th adapter attaches directly to the microscope stan and permits the camera to be swung in and ou of position over the eyepieces. The prism com pensating system, which renders the camera par focal with the optical system of the microscope, enables three-dimensional images to be photographed without distortion. The camera is easily and quickly operated; a cable release snaps the shutter when the camera is swung into position over the eyepieces.
PRODUCER: American Optical Company, Instrument Division, Buffalo.



• U-V (ULTRAVIOLET) PHOTOMICROSCOPE

DESCRIPTION: Used to examine and to make photo records of cells under ultraviolet light, this instrument incorporates an ultrascope tube which permits visual focusing. The ultrascope tube, an electronic component developed by Radio Corporation of America, receives the ultraviolet image at one end and converts it to a visible image, which is viewed under magnification at the opposite end. The photomicroscope unit is easily portable and includes microscope, U-V optics, and image converter. The Grating Monochromator is offered as an accessory. An image converter unit consisting of an ultrascope tube and 35 mm. camera is also available for use on standard monocular microscopes.
PRODUCER: Bausch & Lomb Optical Co., Rochester, N.Y.


spare needless urinary pain
Within 30 minutes, Pyridium's unusually prompt analgesic action will spare needless pain and help overcome resistance to urological procedures. When prescribed for home use, Pyridium encourages more normal micturition by removing the penalties of pain and burning.
DOSAGE: *Adults:* 2 tablets, (100 mg. each), three times daily, before meals. *Children 9 to 12 years:* 1 tablet three times daily before meals.
WARNER CHILCOTT
MORRIS PLAINS, N.J.
PYRIDIUM®
(brand of phenylazo-diamino-pyridine HCl)

THE MEDICAL *Bookman*

► DIFFICULT DIAGNOSIS

By H. J. Roberts, M.D., Staff, Good Samaritan and St. Mary's Hospitals, West Palm Beach, Florida. 913 pages with 99 illustrations. 1958, W. B. Saunders Company, Philadelphia and London. $19.00.

In the practice of medicine, the illnesses of most patients are more or less readily diagnosed. Occasionally, however, the physician is confronted with a difficult diagnostic problem. This text was designed as an aid to diagnosis and deals primarily with uncommon diseases and unusual manifestations of common diseases. As the author states in the introduction, the text is not intended to cover the usual manifestations of common diseases or to be a comprehensive discussion of all diseases. It can be used to greatest advantage in conjunction with one of the standard texts on medicine.

The book is divided into two parts. The first includes chapters on endocrine disease, metabolic disorders, diseases of the heart and vessels, collagen diseases, neoplasms, iatrogenic illness, postoperative complications and many other subjects. The chapter on cutaneous medicine contains an extensive atlas of excellent illustrations.

Part 2 features reviews of many procedures and tests that may be helpful in diagnosis. The various technics are grouped into chapters concerning blood chemistry; hematologic, renal, hepatic and endocrinologic studies; exfoliative cytology and other subjects. The normal range is given for each procedure, as well as the technical factors which may alter the test or its interpretation and a brief discussion of the conditions under which the test may be helpful in diagnosis.

R. V. R.

► RECENT ADVANCES IN PAEDIATRICS

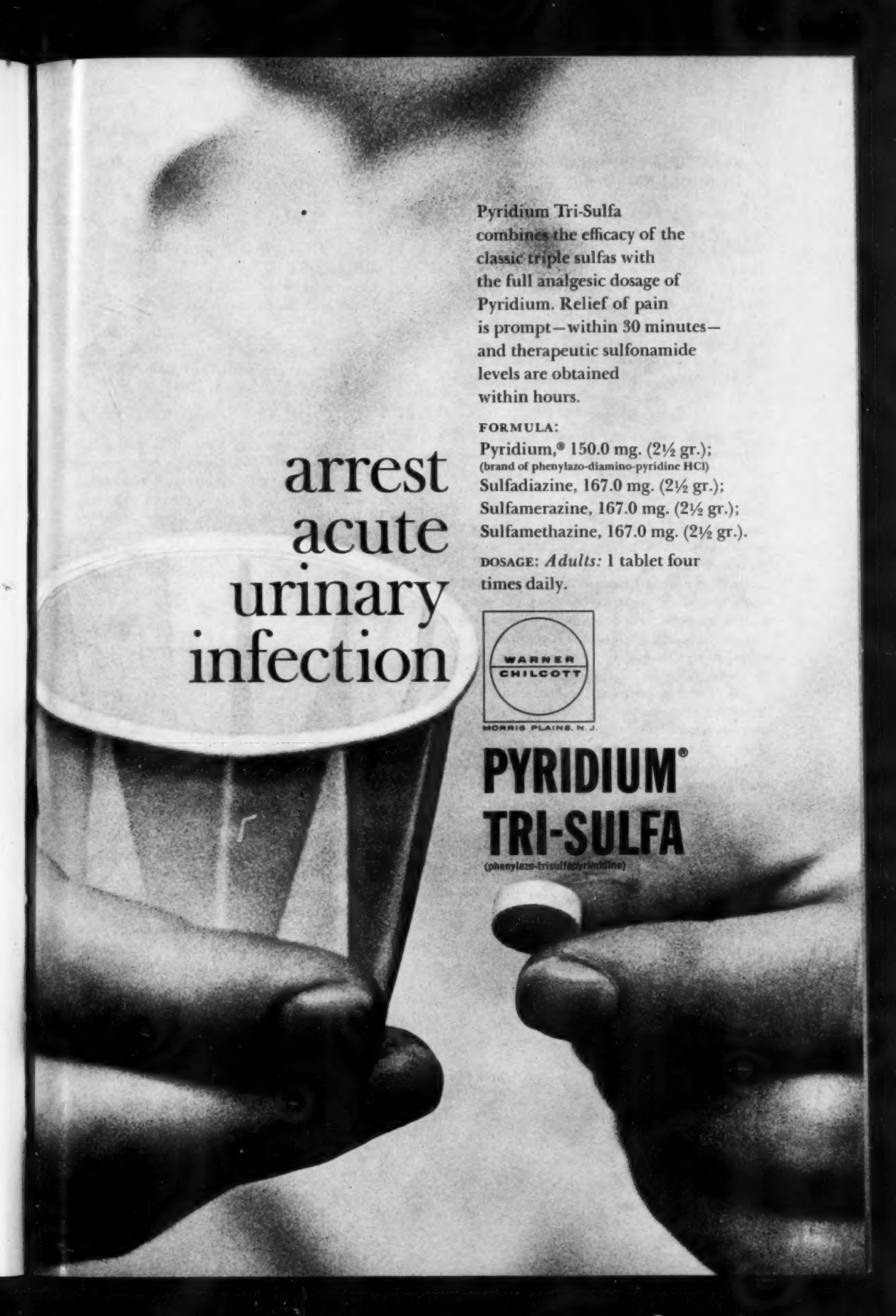
Edited by Douglas Gairdner, M.D., Associate Lecturer in Paediatrics, University of Cambridge, Cambridge, England, with 15 contributors. Ed. 2. 378 pages with 82 illustrations. 1958, Little, Brown & Company, Boston and Toronto. $9.50.

Of the 15 contributors to this collection of monographs, all but three are British. The editor, a well-known pediatrician, has purposely selected material of theoretical as well as practical interest. He notes the slackening in the pace of clinical pediatrics and the entrance into the era of pediatric research, which depends on the basic sciences such as embryology, genetics, physiology and biochemistry in addition to comparative and veterinary medicine. The material in this volume reflects this change in emphasis.

Problems of the newborn infant are considered in chapters on circulatory changes at birth, the hematology of infancy, obstructive and nonobstructive jaundice in the newborn period, spina bifida cystica, and the management of hydrocephalus. Physical growth, tuberculosis, rheumatic fever, pyogenic osteitis and the nephrotic syndrome are discussed, and one author has reviewed problems involving the deaf child.

S. D. M.

(Continued on page A-156)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► ELECTROLYTE CHANGES IN SURGERY

By Kathleen E. Roberts, M.D., Assistant Chief of Medicine, United States Public Health Service Hospital, San Francisco; Parker Vanamee, M.D., Assistant Attending Physician, Memorial Hospital for Cancer and Allied Diseases, and J. William Poppell, M.D., Chief, Section of Cardiopulmonary Physiology and Associate, Sloan-Kettering Institute for Cancer Research, New York. American Lecture Series. 113 pages with 21 illustrations. 1958, Charles C Thomas, Springfield, Illinois. $4.50.

The problems associated with fluid and electrolyte management are becoming more complex not only because the indications for surgery have broadened, but also because various forms of medication, especially steroids, are being used increasingly. This short monograph covers only one facet of the problem, namely, electrolyte changes in surgery.

The material is based on the authors' experiences with 1500 patients who had various electrolyte changes and on results of experiments in more than 2000 animals. The subject is presented from a practical viewpoint, and much controversial material is eliminated.

The effects of preoperative preparation on the electrolyte pattern are presented first. This section covers the effects of various purgatives and enemas and the change caused by diarrhea. The effects of blood volume replacement are considered from the standpoint of both massive transfusion and overtransfusion. The discussion of the various factors involved is of special value to the surgeon who deals often with these situations.

Of utmost importance to the surgeon is the postoperative change in water and electrolyte balance. While this aspect has been covered in a rather straightforward manner, it has by no means been oversimplified. The authors consider the various changes, their explanation when known, and treatment. The well-written section on the alteration in acid-base balance is the largest single section of this book. Numerous referrals to recent publications are made, and in some instances charts are reproduced and explained in detail.

The book concludes with short discussions of complications from physiologic alterations due to the removal of gastric or intestinal segments or to hepatic failure and following operations on the urinary tract in which ureteral transplants are made or renal shutdown occurs.

Y. S.

► ETIOLOGY AND TREATMENT OF LEUKEMIA
Proceedings of the First Louisiana Cancer Conference

Edited by Walter J. Burdette, M.D., Professor and Head, Department of Surgery, University of Utah College of Medicine, Salt Lake City. 167 pages, illustrated. 1958, The C. V. Mosby Company, St. Louis. $4.00.

The presentations and discussions recorded in this volume provide an introduction to research activities related to current etiologic and chemotherapeutic concepts about leukemia. The subject matter includes reviews of the measures used in selecting agents for clinical trial. Etiologic concepts based on work with experimental animals are extensively presented, but relatively less attention is accorded the problems of clinical diagnosis and palliative treatment.

T. C.

► COLLECTED PAPERS
Through Paediatrics to Psycho-analysis

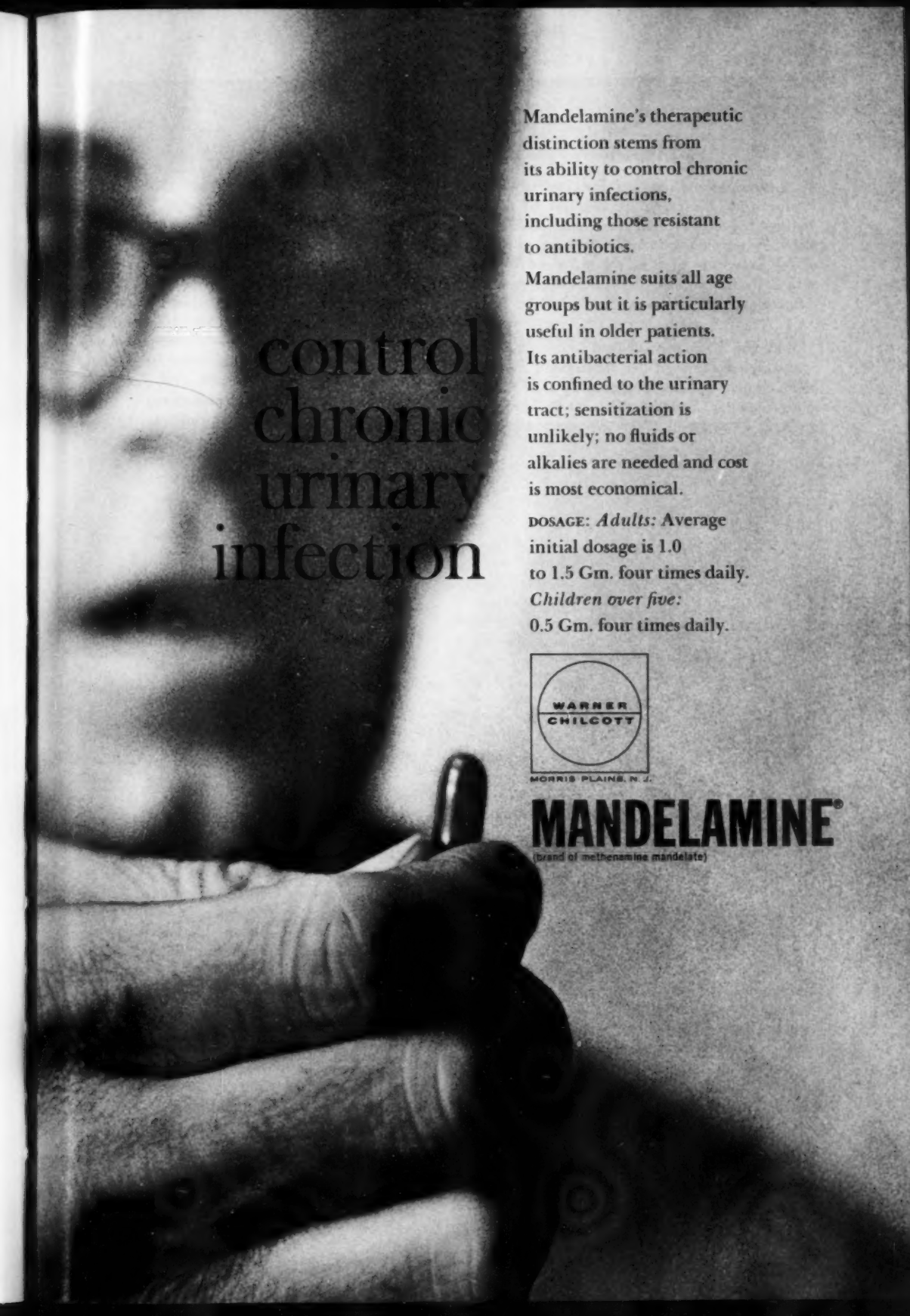
By D. W. Winnicott, M.D., London, England. 350 pages. 1958, Basic Books, Inc., New York. $6.00.

In 1923 Dr. Winnicott became a pediatrician in the Paddington Green Children's Hospital, London; at the same time he was psychoanalyzed. He then applied psychoanalysis to his pediatric practice and has held high positions in both fields.

His collected papers begin with writings as far back as 1931 and represent a great deal of thought as to the basis of mental disturbances in children and infants. The essays are somewhat lacking in continuity, their greatest value lying in the carefully considered case reports. However, these often come to naught because they represent problems apparently too deep for conclusion. The writing is straightforward and the presentation is honest.

M. F.

(Continued on page A-158)



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► THE PHYSIOLOGY AND PATHOLOGY OF THE CEREBELLUM

By Robert Stone Dow, M.D., Associate Clinical Professor of Medicine, University of Oregon Medical School, Portland, and Giuseppe Moruzzi, M.D., Professor and Head, Institute of Physiology, University of Pisa, Pisa, Italy. 675 pages with 185 illustrations. 1958, The University of Minnesota Press, Minneapolis. $12.50.

Since this book was planned to complement a companion volume on the anatomy of the cerebellum which is being prepared by Olaf Larsell, many anatomic features deliberately have been omitted. The first of the two parts of this text, by Dr. Moruzzi, deals with the physiology of the cerebellum. It is a monumental review of the contributions which have been made in this field, especially since the work of Luciani around 1891. Considered separately and extensively are the results of ablation, stimulation and electrophysiologic experiments and the relationship between the cerebellum and other central structures. Each chapter of the review is summarized, and an additional chapter sums up the current knowledge and lack of knowledge of the function of the cerebellum. The author states, "On the whole our feeling is that the time is not yet ripe for any attempt to formulate a new concept of cerebellar functions." Those not possessing a good background in neurophysiology may well find this part of the book heavy going. The clinician naturally regrets that Dr. Moruzzi does not believe that accurate simplified generalizations of cerebellar functions are presently possible.

The second part of the book, by Dr. Dow, is devoted to the clinical symptomatology and the diseases affecting the cerebellum, with extensive reference to the literature on the subject. The approach is that of a clinician with good experience in cerebellar diseases. The illustrations of histopathology have a supporting rather than a primary function. Clinical symptoms and signs occurring with cerebellar and related lesions are admirably treated, and the discussions on developmental anomalies and acute inflammatory and toxic disorders are extensive and well done. The chapter on atrophic disease of the cerebellum follows classic lines. Other chapters deal with chronic infections and abscesses, vascular disease, trauma and tumors involving the cerebellum.

J. R. B.

► THE YEAR BOOK OF PEDIATRICS (1958-1959)

Edited by Sydney S. Gellis, M.D., Professor and Chairman, Department of Pediatrics, Boston University School of Medicine, Boston. 496 pages with 125 illustrations. 1958, The Year Book Publishers, Inc., Chicago. $7.50.

This well-recognized volume contains reviews of the pediatric literature published in American and foreign journals between May 1957 and May 1958. The material is of current interest and provides a means by which the busy practitioner may readily familiarize himself with the newest knowledge in any branch of pediatrics.

To facilitate location of information, the book is divided into chapters concerned with the various organ systems. Also considered are the premature and the newborn infant, nutrition and metabolism, infectious disease and immunity, tumors, toxicology and therapeutics. The comments following many of the reviews provide some of the most interesting reading in the book and serve to evaluate controversial material. Anyone who has used previous editions will be pleased with the quality of this one.

S. D. M.

► THE CARE OF THE GERIATRIC PATIENT

Edited by E. V. Cowdry, Ph.D., Director of Wernse Cancer Research Laboratory, Washington University School of Medicine, St. Louis, with 22 contributors. 438 pages. 1958, The C. V. Mosby Company, St. Louis. $8.00.

In this volume well-known authorities discuss the psychologic, medical and surgical aspects of the care of geriatric patients. The text includes excellent chapters on rehabilitation and on dental, nursing, hospital and nursing-home care, as well as information about anesthesia, drugs and nutrition.

Each chapter is short and to the point and is followed by a list of references for the reader who wishes to obtain further knowledge.

Although this book is not voluminous, numerous suggestions by the contributors make it a useful addition to the library of anyone interested in geriatric problems and care.

I. P. F.

(Continued on page A-160)

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Reference: 1. Garrett, T. A.: Clin. Med. 3:1185, 1956. 2. Cavallito, C. J., and Jewell, R.: J. Am. Pharm. A. (Scient. Ed.) 47:165, 1958. 3. Cavallito, C. J., and O'Dell, T. B.: J. Am. Pharm. A. 47:160, 1958. 4. Report on a New Repository Principle, Med. Sc. 3:376, 1958.

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► HEREDITY OF THE BLOOD GROUPS

By Alexander S. Wiener, M.D., Senior Bacteriologist (Serology) to the Office of the Chief Medical Examiner of New York City, and Irving B. Wexler, M.D., Associate Pediatrician, Jewish Hospital, Brooklyn. 150 pages, illustrated. 1958, Grune & Stratton, Inc., New York and London. $6.00.

This is a remarkably concise and clear presentation of the principles of blood group serology, with special emphasis on the genetic determination of the presence of red cell agglutinogens. In spite of the monograph's brevity, there is no tendency toward oversimplification. The subject matter is as up to date as is possible in this rapidly developing field and includes discussions of additional knowledge of blood groups published as recently as 1957. The work as a whole reflects to a large extent the numerous original and valuable contributions of the senior author, including certain theories and viewpoints, such as the differentiation between agglutinogens and blood factors or blood factor C which is postulated to be common to A and B agglutinogens, that are not shared by other workers in the field.

In addition to the ABO and Rh-Hr systems, the MNS, P, Kell, Lutheran, Duffy and Kidd blood groups are discussed, although in less detail. Because of their relationship to the secretor property, the Lewis blood groups are considered jointly with the ABO system. The chapter on medicolegal applications of blood group tests is of special value and contains informative tabular material on the chances of excluding paternity by the use of one or more of the blood group systems and by demonstrating the presence of particular blood factors in the individual falsely accused of paternity.

The text also includes an extensive discussion of the differences in the genetic and immunologic implication of the Wiener Rh terminology and the Fischer-Race CDE notations. While data pointing to the theoretical validity of Wiener's concepts are convincingly presented, the authors have unfortunately repeated an earlier statement by Wiener in which he insists that ". . . the original Rh-Hr notations be retained as the standard and sole nomenclature for the preparation of approved medicolegal reports on Rh types." This statement is followed by the recommendation to do likewise in clinical medicine and anthropology. Even granting the theoretical validity of Wiener's nomenclature, it appears unrealistic to expect that the Fischer-Race notations, which are used almost exclusively in Europe as well as by some American authors, could be completely eradicated.

In discussing the degree of expertness in immunohematology needed to engage in medicolegal tests, it is especially unfortunate that the following statement by Wiener is quoted: ". . . those who find it necessary to resort to the incorrect CDE notations . . . do not understand the subject thoroughly, and . . . this may be used as one of the criteria by which to judge the qualifications of an expert." Incidentally, the authors' use of additional blood group symbols which deviate from the generally accepted ones, such as F for Fy^a and J for Jk^a, may lead to further complications in blood group notations. These points are, however, minor drawbacks in an excellent book.

K. S.

► CONVULSIVE DISORDERS OF CHILDREN

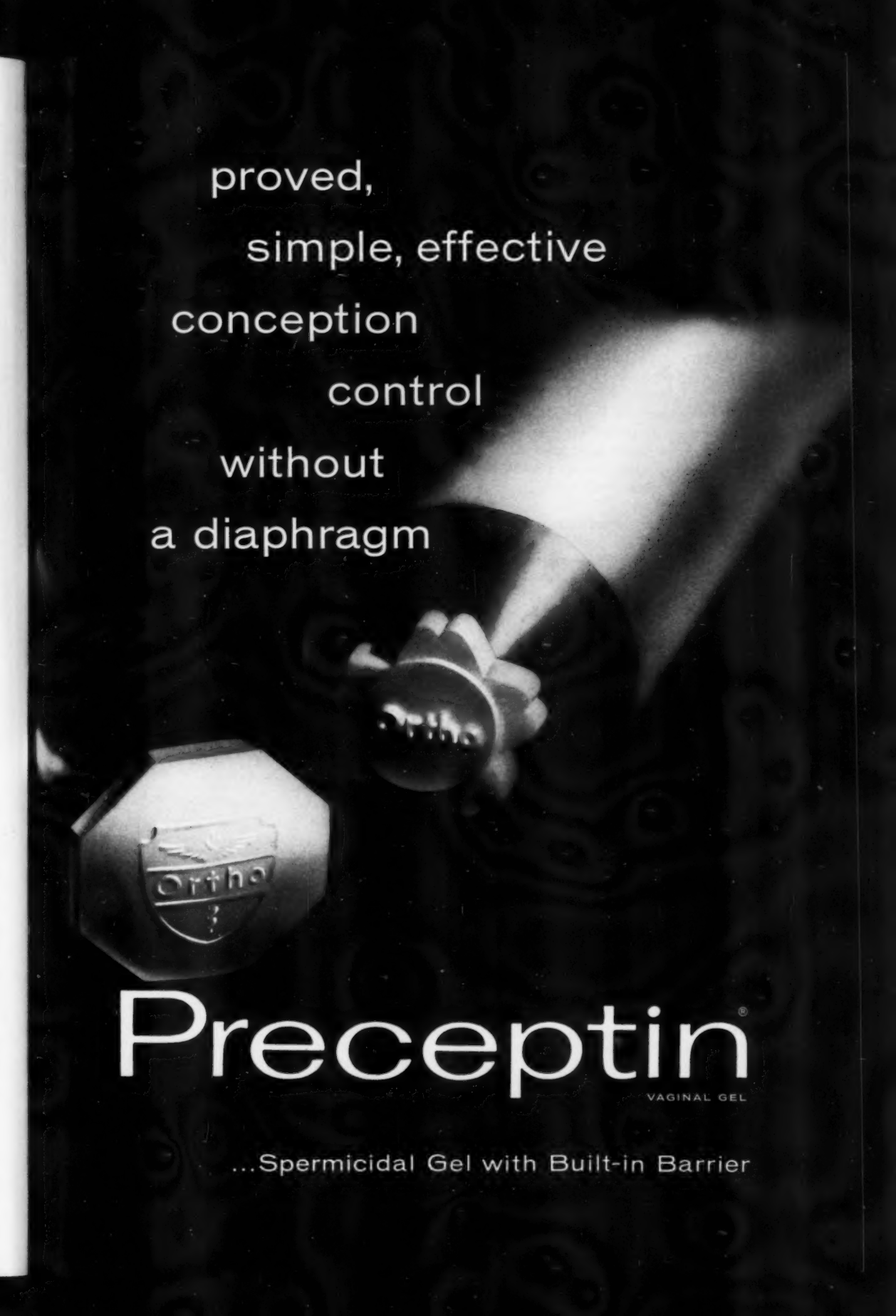
By Dora Hsi-Chih Chao, M.D., Assistant Professor of Pediatrics and Neurology, Ralph Druckman, M.D., Assistant Professor, Departments of Neurology and Physiology, and Peter Kellaway, Ph.D., Associate Professor, Department of Physiology, Baylor University College of Medicine, Houston. 151 pages with 25 illustrations. 1958, W. B. Saunders Company, Philadelphia and London. $6.00.

According to the authors, this book is a revised version of a manual on convulsive disorders originally prepared for the use of residents in the Blue Bird Circle Children's Clinic in Houston. It deals in an orderly and easily readable manner with present-day knowledge of the subject.

In the introduction, the problems, definitions and classifications are clearly outlined. Most chapters are brief but they contain essential information. As might be expected, the chapter on electroencephalograms contains considerable detail with excellent illustrations of the various types of tracings encountered. Therapy is outlined, and a table is included which shows the various drugs that can be used and the amounts to be given at various ages.

H. M. K.

(Continued on page A-162)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► METABOLIC DISTURBANCES IN CLINICAL MEDICINE

Edited by G. A. Smart, M.D., Professor of Medicine, University of Durham Medical School, Newcastle upon Tyne, England, with 14 contributors. 358 pages with 35 illustrations. 1958, Little, Brown & Company, Boston. $10.00.

Each chapter of this unique book is written by one or more English or American authors who are experts in their respective fields. The various chapters deal with general nutrition; water, electrolytes, and aldosterone; renal disease; injury; hepatic disease; cardiovascular aspects of metabolic disease; edema in congestive heart-failure; atherosclerosis; pulmonary function and acid-base balance; oxygen therapy; metabolic bone disease; the hematopoietic system, and the central nervous system.

The text is well written and up to date, and a brief bibliography follows each section.

This book is highly recommended to those who are interested in the metabolic abnormalities present in disease.

R. V. R.

► CALLANDER'S SURGICAL ANATOMY

By Barry J. Anson, Ph.D., Chairman, Department of Anatomy, and Walter G. Maddock, M.D., Edward S. Elcock Professor of Surgery, Northwestern University Medical School, Chicago. Ed. 4. 1,157 pages with 1,047 illustrations. 1958, W. B. Saunders Company, Philadelphia and London. $21.00.

Many medical educators consider this the standard textbook on surgical anatomy. The material is presented in the pattern of previous editions. Emphasis is on the rationale of the surgical approach rather than on technic. Understandably, the latter feature is desirable since surgical technics change, whereas human anatomy varies only within predictable limits. Further studies and observations on anatomic variations are new in this edition.

In general, chapters are arranged according to regional anatomy. Following a detailed description of the anatomy, the various diseases, congenital defects, and injuries usually treated by surgery are illustrated and described in detail. Advantages of the different types of surgical approach are listed; in many instances, difficulties encountered by different anatomic approaches are explained.

All the illustrations are artist's drawings, featuring a clear and concise description of the incision, the sequence of structures encountered and the manner and direction of retraction necessary for exposure of the surgical site. This, of course, is the essential difference between a surgical anatomy book and a textbook on anatomy in which only structure is illustrated. Furthermore, when deep structures are shown in the latter, the superficial structures are not illustrated.

The description of the lung is rather inadequate. The present concept of the segmental anatomy of the lung is treated only superficially, and the relationship of the pulmonary artery and venous system to the segmental anatomy is completely omitted. Today the knowledge of these relationships is indispensable to thoracic surgery. Complete books on this subject are available, and it seems that more of this material should have been included in this text. Surgical anatomy and approaches for cardiovascular surgery are also rather incomplete.

In sharp contrast to the deficiencies in the section on the thorax, other sections such as those on the abdomen and the extremities are almost encyclopedic.

Y. S.

► THE BORDERLAND OF EMBRYOLOGY AND PATHOLOGY

By R. A. Willis, M.D., Emeritus Professor and Honorary Research Fellow in Pathology, University of Leeds, Leeds, England. 627 pages with 244 illustrations. 1958, Butterworth and Co. (Publishers) Ltd., London, England. $18.00.

The title of this book clearly indicates its unique place in medical literature. The well-known author has brought together his own experiences and, with voluminous references, has endeavored to present many accumulated facts in their proper relationship. Both embryologists and pathologists will find it a valuable reference.

The paper and typography and the literary style of this scholarly author make for a delightful book. Larger medical libraries will surely own it.

A. H. S.

(Continued on page A-164)

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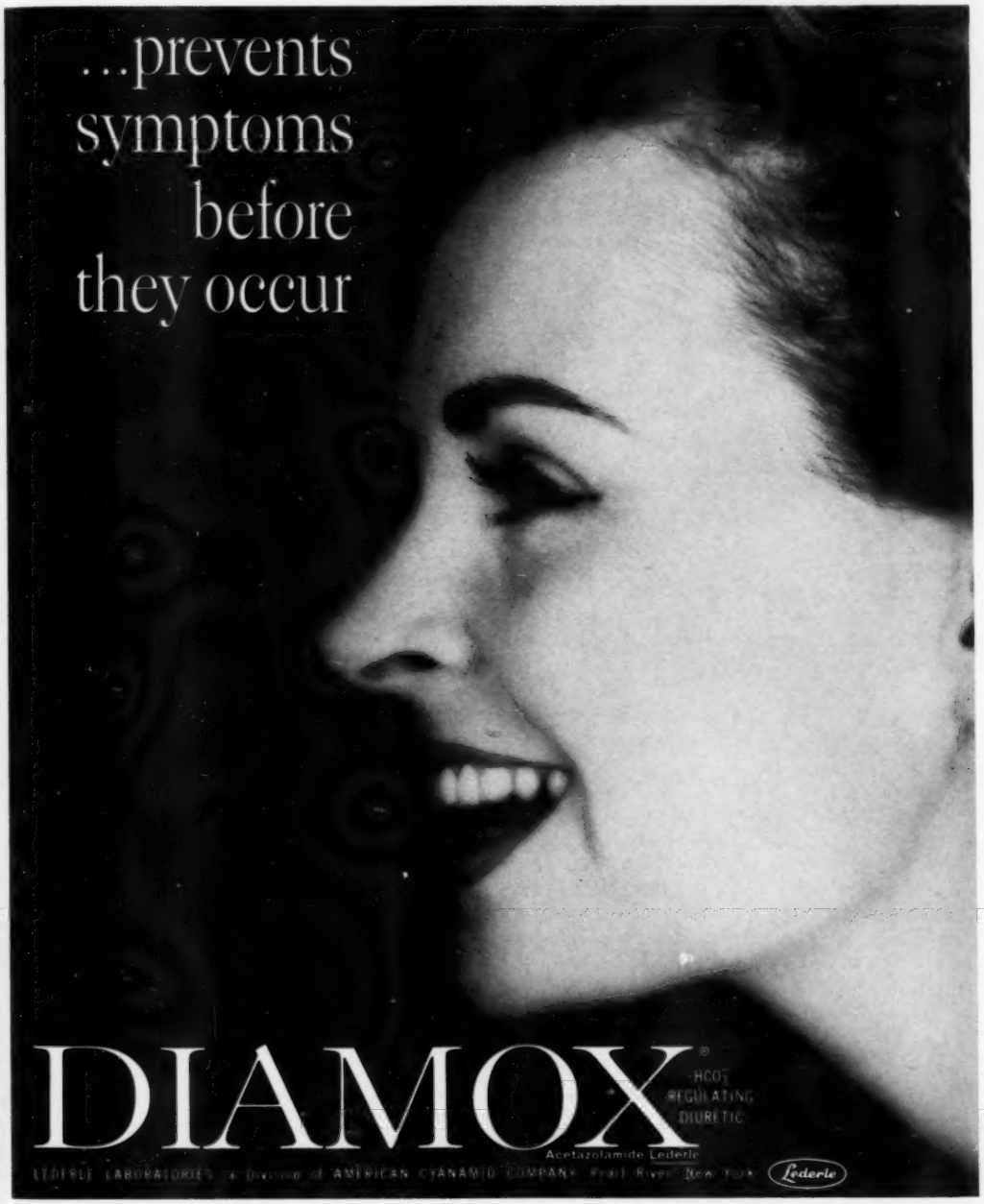
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► POISONING
A Guide to Clinical Diagnosis and Treatment

By W. F. von Oettingen, M.D., National Institutes of Health, Public Health Service, U. S. Department of Health, Education and Welfare, Bethesda. Ed. 2. 627 pages. 1958, W. B. Saunders Company, Philadelphia and London. $12.50.

Six years have passed since the first edition of this work was published. During this interim new types of poisoning have been reported, new methods have been devised for the detection of toxic materials in biologic specimens, and new procedures in the treatment of poisoning have been proposed. The advent of new therapeutic agents, some with potentially dangerous side effects, has necessitated a more detailed description of the side actions which do not represent actual poisoning, but the knowledge of which is extremely important to correct diagnosis and proper treatment. The author has revised the list of chemicals and poisons causing certain functional changes, emphasizing the more characteristic symptoms and omitting minor ones.

Initial chapters cover classification and diagnosis of poisoning, medicolegal responsibilities, and emergency measures and equipment. When discussing diagnosis, the author stresses an adequate history of the patient, structural and functional pathology, biochemical changes and laboratory tests. The section on management of these conditions reviews the rationale of treatment, removal and elimination of the toxic agent, detoxification of the absorbed poison, and treatment of symptoms and aftereffects. Concluding chapters deal with symptoms and treatment of the various types of poisoning and toxic reactions to drugs.

A bibliography with the important current literature appears at the end of each review of a drug or chemical. Although this book is not intended to give a detailed toxicologic method for the identification of these various chemicals, there are ample discussions of the importance of clinical findings, the direct and differential diagnosis, and the similarity of clinical changes between the drug in question and related drugs.

This excellent text can be highly recommended to all members of the medical profession and should be available to medical and nursing staffs in hospitals.

S. A. L.

Books received are acknowledged in this department. As space permits, books of principal interest to our readers will be reviewed more extensively. Additional listings will be found on pages 282 and 294 of this issue.

Elements of Biophysics. By James E. Randall, Ph.D., Associate Professor of Physiology and Biophysics, University of Missouri School of Medicine, Columbia. 346 pages, illustrated. 1958, The Year Book Publishers, Inc., Chicago. $8.00.

Behaviour and Physique; an Introduction to Practical and Applied Somatometry. By R. W. Parnell, D.M., Research Physician in the Constitutional Aspects of Psychiatric Medicine, The Warneford Hospital, Oxford, England. 134 pages, illustrated. 1958, Edward Arnold (Publishers) Ltd., London. Distributed in the United States by The Williams & Wilkins Company, Baltimore. $7.00.

The Amphetamines; Their Actions and Uses. American Lecture Series. By Chauncey D. Leake, Ph.D., Professor of Pharmacology, Ohio State University, Columbus. 167 pages. 1958, Charles C Thomas, Springfield, Illinois. $4.50.

Understanding Aphasia. A guide for family and friends. By Martha L. Taylor, M.A., Chief, Department of Speech and Hearing Therapy, Institute of Physical Medicine and Rehabilitation. No. 2. 48 pages, illustrated. 1958, Institute of Physical Medicine and Rehabilitation, New York University-Bellevue Medical Center, New York. $0.50.

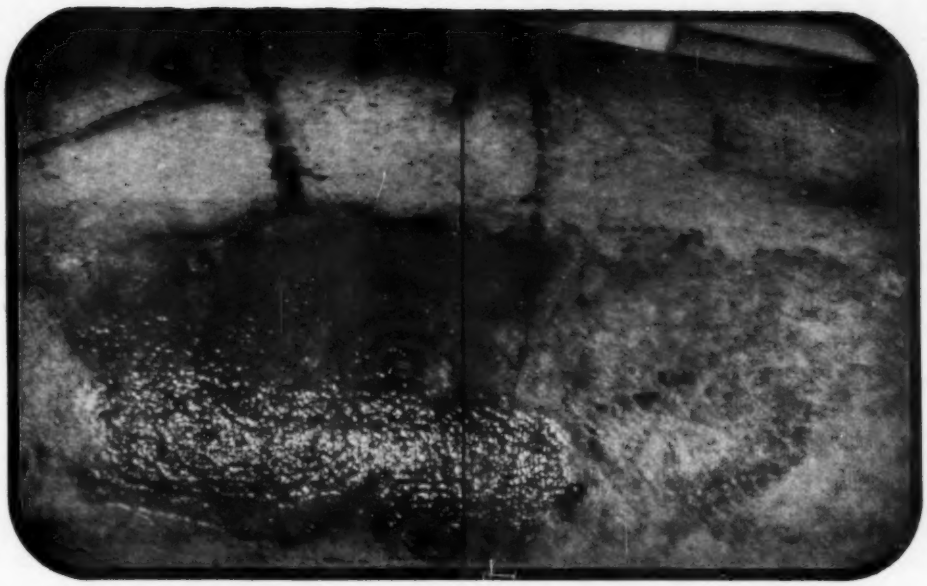
Breast Cancer. The second biennial Louisiana Cancer Conference. Edited by Albert Segaloff, M.D., Associate Professor of Clinical Medicine, Tulane University School of Medicine, New Orleans, with 30 contributors. 257 pages with 42 illustrations. 1958, The C. V. Mosby Company, St. Louis. $5.00.

Amid Masters of Twentieth Century Medicine. By Leonard G. Rowntree, M.D., formerly, Chief of Medicine, Mayo Foundation, Rochester, Minnesota; presently, Chairman, Medical Advisory Board, The American Legion. 684 pages, illustrated. 1958, Charles C Thomas, Springfield, Illinois. $11.50.

Carcinoma of the Lung. Series of monographs on neoplastic disease at various sites. Edited by J. R. Bignall, M.D., Assistant Physician, Brompton Hospital, London, England. Vol. 1. 298 pages, illustrated. 1958, E. & S. Livingstone Ltd., Edinburgh and London. Distributed by The Williams & Wilkins Company, Baltimore. $10.50.

Amino Acids and Peptides With Antimetabolic Activity. Ciba Foundation Symposium. Edited by G. E. W. Wolstenholme, O.B.E. and Cecilia M. O'Connor, B.Sc. 286 pages with 28 illustrations. 1958, Little, Brown & Company, Boston. $8.75.

Neurological and Psychological Deficits of Asphyxia Neonatorum. Edited by William F. Windle, Ph.D., Chief of the Laboratory of Neuroanatomical Sciences, National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda. 336 pages with 83 illustrations. 1958, Charles C Thomas, Springfield, Illinois. $8.00.



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Jeffords, J. V., and Hagerty, R. F.: Ann. Surg. *145*:169, 1957.

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DR. Pepys' Pages

Personal Diary
and Observations on
Medical Life
by MORRIS FISHBEIN, M.D.

Jan. 1—Early awake and wishing Mistress Pepys a healthful and happy new year. Then almost all the day at television, viewing the Rose Parade and the bowl games, and at night reading "The Big Gamble," by Coxe, a mystery involving newspaper photographers and replete with new technical information on detection.

Jan. 2—At the desk, with my mail, the post office catching up with deliveries but not equaling the long-distance telephone, which increasingly takes over communications. Then dictating on the books of cardiology.

Jan. 4—Reading "Kill My Love," by Kyle Hunt, a British "whodunit," psychologically set up to show that crime does not pay. Also observing TV grown-up with the Aeschylus "Orestes," a view of China, and "Meet the Press," with Senators Paul Douglas and Javits.

Jan. 5—At 7 A.M. off to Cincinnati, and there sat in the airport five hours waiting to leave for Winston-Salem. Read Ellery Queen's "The Finishing Stroke," which is built around a famous carol about the 12 days of Christmas and goes one better over mysteries dependent on twins by bringing in triplets. At the airport met by student Armstrong, and to Staley's Steak House for a fine dinner with the student committee accompanied by Drs. Burt and Wingate Johnson. Next for photographs and an interview in the library of Bowman Gray School of Medicine of Wake Forest College, and to speak to an assemblage of students and faculty. Thereafter a reception at the home of obstetrician Burt, and then to sleep at a fine motel, without heat at a temperature of 5° above zero.

Jan. 6—Home on schedule and at the desk, and in the evening to dine at Imperial House, celebrating the twenty-fifth anniversary of the Kirsners as guests of Joel Goldblatt and his charming and talented Lynn.

Jan. 7—In the afternoon came Leon Levy and Resnick to plan for the National Jewish Hospital in Denver, and after dinner Mistress Pepys and I were again defeated mathematically by my brother Albert.

Jan. 8—To the Museum of Science and Industry for a meeting of the medical advisory board with Major Lohr and McMaster, Tom Jones, Hull, Longenecker, Spence and many more. So discussed exhibits and public health education. Then to dine at the Standard Club, and to the orchestra, where the visiting director from Zurich, Hans Rosbaud, went on a binge of neomodern music.

Jan. 9—Amid the turmoil of writing, and read "Parrish," by Mildred Savage, an engrossing novel of the cigar tobacco industry, with one of those tyrannical fathers who ruins his family by his despotism and makes his children either rebellious or lacking in will and spirit. At night to dine at the Standard Club and then to the opening of the Beryozka Russian dancers.

Jan. 10—At the desk, the library and the bank. At night to the Beau Nash room in the Ambassador, where classmate L. D. Smith and Rose entertained for a fine evening with good food, good company and a mathematical disaster with Green, Greenfield and Lahr. Among these experts old Pepys looked green too.

Jan. 12—Working with Grimes of the Heart Association on home care, heart attacks and ambulance services.

Jan. 13—By the noon plane to New York and at night to "21" with the Bill Lasdon family, and saw there Milton Biow and Melisse.

Jan. 14—Early to Morris Plains, meeting with Al Driscoll and Len Scheele, Ellwood Douglass and Paul Robinson. In the late afternoon to Doubleday for talks with Black, Runyon and Beebe. At night to dine with the B. A. Goodmans, Alice making a great hostess. Here were Gordon Heyd, Hortense Powdermaker, Admiral Knickerbocker and his lady, and Paul Warwick and his charming mate.

Jan. 15—To Warwick and Legler for more meetings, where were John Welsh, Fred Baldwin, George Mosely and Dr. Beckley. And next to Herbert Mayes of *McCall's*, finding him full of enthusiasm and drive in his new work. For luncheon with Max Geffen and Paul Robinson at the RCA Club, talking of new magazine projects. After a visit to Taylor-Carlisle's bookstore, came

(Continued on page A-196)

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FOR ARTHRITIS

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Effective and well tolerated on the practical dosage of only 6 tablets daily,
PARAFON and PARAFON WITH PREDNISOLONE provide benefits that last for up to six hours.

PARAFON relieves pain, stiffness, and disability caused by rheumatism and traumatic disorders; PARAFON WITH PREDNISOLONE compounds this relief with anti-inflammatory action in treatment for arthritis.

supplied: PARAFON: Tablets, scored, pink, bottles of 50. Each tablet contains: PARAFLEX Chlorzoxazone† 125 mg.; and TYLENOL® Acetaminophen 300 mg.
PARAFON WITH PREDNISOLONE: Tablets, scored, buff colored, bottles of 36. Each tablet contains: PARAFLEX Chlorzoxazone 125 mg.; TYLENOL Acetaminophen 300 mg.; and prednisolone 1.0 mg.

precautions: The precautions and contraindications that apply to all steroids should be kept in mind when prescribing PARAFON WITH PREDNISOLONE.

[illegible]

McNEIL

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Bert Berne of *Dunn's Review* for more conference. Thereafter to the Drake Hotel for dinner with the Runyons and then to see "La Plume de Ma Tante," which is the current hit, full of rough humor.

Jan. 16—Conversing with Tom Rivers of the work of the National Foundation. Then for some time with "Bud" Gruber and Dr. Parmele of P. Lorillard. In the afternoon came the Van Ripers, with great news of their offspring, and Peter Warren, still riding the crest with *Excerpta Medica*. At night to Milton Biow's for a dinner with the Max Raabs and Herman Sondheims, with fine talk of medicine, public affairs and the theater until midnight.

Jan. 17—Early to the Queen Mary to cabin M-81, where the Runyons entertained with champagne before sailing, and here were all the neighbors—Unkie, Black, Sherman, Tom Costain, the great writer, and all the ladies. Next to see Billy Rose in his magnificent mansion to talk about a foundation, and viewed his collection of Epstein sculptures and the Dali etchings in the elevator. Next to luncheon with the Sorokos, after which a tight gin game. After cocktails at Bill Lasdon's, with the Lasdon and Freiwald families, to dine at the Pierre and hear a review of the talented Jerome Kern's songs. The feature of the evening was announcement of the engagement of Nan Lasdon Laitman to Dr. Milton Freiwald.

Jan. 18—Early came Milton Freiwald to confer on some glaucoma research. Then to Idlewild to fly to Chicago, and en route read two paperback mysteries which were quickly forgotten.

Jan. 19—At the desk reading all the magazines, with much editing and correspondence and several visitors, so that when evening came happy to go early to rest and read "Young Love," from the Danish by Johannes Allen, which shows Danish youth—as the young everywhere—in revolt, doubtful of the future, and striving to squeeze out of life every possible moment of pleasure. And also "Lady L," by Romain Gary, which is a weird story of anarchists, great ladies, intrigue and sentiment, beautifully written.

Jan. 20—In the midst of the snow to the Rotary Club to hear a lecture on Rotary and was introduced through chance seating by the secretary of the American Osteopathic Association, Eveleth. Then came a blizzard, and journeyed to the Tavern Club to dine with the Bob Hardts and the Friedells and chatted a while with Charles Lipscomb.

Jan. 21—At the desk until noon and then to the funeral of Ernest Irons, whom I had known well since 1910, when we worked in the McCormick Institute for Infectious Diseases. Through the years, during which he achieved among the highest honors of medicine, he was scrupulously honest, ardent in his love for Rush Medical College, and had courage to fight for the right.

Jan. 22—Four degrees below zero as an aftermath of the blizzard. Read "The Man Who Disappeared," by Edgar Bohle, another tale of a scientist kidnaped and brainwashed by Communists, strong on suspense. At night to hear conductor Previtali with the symphony, and enjoyed particularly some Italian compositions played to half an audience because of the cold—but the Charles Huggins family and ours made it.

Heard of two cows standing beside a fence in a pasture as a milk truck rumbled by. On the truck was a sign: "Grade A Milk, Pasteurized, Homogenized, Fortified With Vitamins A and D." The older cow began to weep. She sobbed: "It makes me feel so inadequate."

Jan. 23—To the Chicago Heart Association, meeting with Turner, Grimes, Hilliard, Stamler and others to work out the home care program for Cook County Hospital. The city is blanketed with snow, so spent the evening reading René Dubos' book, "Mirage of Health," which is profound, philosophical, erudite and exciting.

Jan. 25—The weather continues miserable, so worked at my scrivening and heard Leonard Bernstein do Gershwin's "Rhapsody in Blue" on "Omnibus." This is the most! Finished "The Scientists," by Eleazar Lipsky, which is good when it could have been great. The *New York Times* critic emphasizes its relationship to the Banting-McLeod insulin discovery, and seems to have missed the story of the Waksman streptomycin patent and its relationship to Rutgers and the new biology center.

Jan. 26—To my tailor who finds me 0.5 in. greater in girth, and thought of the comedian who said his girl was 44-24-34, but not in that order. Next to the Drake to talk for an hour with the great Bernardo Houssay of events in Argentina, he being here with President Frondizi. And heard of the sudden death of Dr. Braun-Menendez in an accident, leaving a wife and 10 children.

(Continued on page A-198)

in cold, aching extremities

ILIDAR

increases peripheral circulation . . .
relieves vasospasm

When cold, numb, aching extremities indicate peripheral ischemia due to vasospasm, ILIDAR offers *prompt* relief through *profound* vasodilation. "The drug proved highly effective in patients with predominantly vasospastic disorders as manifest by coldness, blanching and aching of the extremities, especially when aggravated by cold weather."[1]

Unlike most vasodilators, ILIDAR is exceptionally well tolerated. "The mildness and infrequency of the side reactions make Ilidar one of the most pleasant drugs in its class to use."[1]

Prescribe ILIDAR to relieve such symptoms of peripheral vasospastic disorders as aching, burning, coldness, night cramps and numbness of the extremities.

Reference: 1. H. D. Green and H. H. DuBose, *Circulation*, 10:374,1954.

SUPPLIED: 25 mg tablets in bottles of 100 and 500 tablets.

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Jan. 27—Conferences with Fred Stenn and Pinckney on medical writing. In the evening to dine at the Palmer House, where the Chicago Heart Association entertained Isaac Starr of Philadelphia. At dinner seated between Louis DeBoer and Emmett Bay. Wright Adams presided and Starr gave the fourth James B. Herrick Memorial Lecture. He spoke on the "Strength of the heart." The hearts of older people are shown by the ballistocardiograph to be weaker than those of the young. And Starr disliked the pathologist who holds the heart in his hand and says, "The heart is normal," when clearly it is not beating.

Jan. 28—For luncheon with Eunice Stevens of Hoeber, to talk of publishing. In the evening came Professor Everett Hughes and his lady from the University to talk of sociology, anthropology and archaeology, intermingled with travel. And finished J. Harvey Howell's tale of modern business called "The Big Company Look," which shows how a business can kill the human qualities in a man.

Jan. 29—At noon to the kick-off luncheon for the Chicago Heart Association—the greatest yet—replete with television stars Sammy Davis and the three weather prognosticators Clint Youle, P. J. Hoff and Culbertson. Also there were Rabbi Louis Mann, Mayor Daley and Emerson Foote. But the heart mover was Willis J. Potts with a dozen children recovered from heart surgery, one who had had cardiac standstill for 45 minutes. Wright Adams told of how the funds are spent, and Mike Wallace interviewed Foote on the reasons for the heart drive. In the afternoon with Grandma Mantel, now almost 91, to see Charles Lawrence, who found her physically like a person of early middle age. At night to hear the symphony conducted by Thomas Beecham, now 81, who gave such gorgeous renditions of Schubert, Mendelssohn and others that the audience responded with a great ovation.

Jan. 30—To visit came the Joestings of Minnesota and the Mantels, en route to Hawaii. In the evening to dine with Carol Gibbs, along with Ernie Klein, Roland Frieder, Allen Grawoig and the ladies, with fine conversation about travel, and at last old Pepys achieved some mathematical success.

Jan. 31—To Marshall Field's, consulting the tailors, and the rest of the day reading proofs of articles, books, editorials and a half-dozen periodicals.

The Medical Muse

RICHARD ARMOUR

SPLIT PERSONALITY

Fee splitting is a frightful thing,
A dreadful thing to do.
Throughout the whole profession it
Is said to be taboo.

And yet I must confess I know,
Among the best M.D.s,
A doctor who goes right ahead
And openly splits fees.

He doesn't like to do it, but
He shrugs, says, "Well, that's life,"
And counting out the cash received,
He splits fees—with his wife.

THEIR BITE IS WORSE THAN THEIR BARK

Much more beset by dogs than most men,
Far more, indeed, than even postmen,
Are doctors who, although it rankles,
Have canines sniffing at their ankles
And dogging every rear and fore step
Between the gateway and the doorstep.
How best to manage? Soothe the critter
With whistled notes? Haul off and hit her?
Walk firmly on, the little distance,
Or stop and bellow for assistance?
A doctor, as he comes a-bounding,
Must take from hounds a lot of hounding,
And, called for heart attacks or babies,
Should take along some shots for rabies.